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PARASYPHILIS OF THE NERVOUS SYSTEM.[1]

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THE following preliminary communication is based upon several lines of work, carried out simultaneously in the wards, and in the bacteriological laboratory of the London Hospital. Each separate research will form later the subject of a paper in this Journal, but we thought it wiser to give a preliminary account of our general conclusions before presenting the various more special and detailed communications.

The results embodied in this paper are based entirely on cases where the serological examinations have been carried out by Dr. Fildes and Dr. McIntosh and the clinical records compiled by Dr. Head and Dr. Fearnsides.

[1] This paper was laid before the Neuropathological Section of the International Medical Congress on August 12, 1913.

We have the greatest pleasure in thanking first of all Professor Bulloch, in whose laboratory the work was carried out. Our thanks are also due to the staff of the London Hospital, more particularly to Dr. J. H. Sequeira and Dr. Cecil Wall, for the unrivalled opportunities they so generously gave us for examining patients under their care. If, however, the name of no physician is mentioned in the report of a case, it may be assumed that the patient was under the care of Dr. Head.

Chapter I.—Clinical Characteristics of Parasyphilis.

The conception of parasyphilis as a morbid process, responsible for a wide series of clinical manifestations, was first formulated by Fournier [8] in 1894 to account for cases, obviously of syphilitic origin, which were not amenable to antisyphilitic treatment. "Ce néologisme," he says, "que je dois à un savant helléniste specifie bien, paraît-il, étomologiquement le caractère des accidents en question, dont le propre est de procéder originairement de la syphilis sans être pour cela cependant syphilitique de nature." He believed that this peculiar post-syphilitic condition was able to evoke a series of diseases, all of which might exist otherwise apart from antecedent syphilis. His conception was thus essentially a clinical one, transferred by implication into the field of pathology.

Fournier did not restrict the term parasyphilis to such diseases as dementia paralytica and tabes dorsalis alone, but believed that some cases of progressive muscular atrophy, epilepsy, infantilism, Little's disease, imbecility, and even certain forms of neurasthenia were all manifestations of the activity of the "parasyphilitic" process. Gradually, however, though the truth of Fournier's conception of the post-syphilitic nature of some of these conditions has been generally acknowledged, the range of activity of parasyphilis of the nervous system has tended to become restricted to tabes dorsalis and dementia paralytica; but at the same time an increasingly large number of complications have been described as occurring in the course of these two diseases.

Thus Dejerine [4] has described the pathological changes associated with muscular atrophy, arising in the course of tabes dorsalis, and Nonne [25] looks upon all cases of primary optic atrophy, which follow syphilis, as an incipient stage of the same disease. Mott [18] thinks it probable that Erb's spinal paralysis and certain cases of amyotrophic lateral sclerosis may be primary post-syphilitic dystrophies; optic

atrophy he looks on as one with tabes dorsalis and dementia paralytica.

Fournier's original view was revived by A. Read Wilson [34] but both the clinical and serological reports in his paper lacked sufficient fulness to support his conclusions.

(1) *Clinical Forms assumed by the Disease.*

Year by year the line, once so firmly drawn between tabes dorsalis and dementia paralytica, grew fainter as soon as the identity of the pathological process underlying the two diseases was recognized. With the invention of the term "tabo-paresis" the boundaries between the two diseases fell; it was recognized that manifestations characteristic of each might occur together in the same patient, and their validity as anything more than convenient terms for groups of signs and symptoms disappeared for ever.

Let us then consider the various phenomena which may make their appearance in the course of dementia paralytica and tabes dorsalis, that is to say, the clinical conditions universally recognized to be due to parasyphilis of the nervous system :—

Dementia and other mental states characterized by destruction of mental capacity; all forms of epileptiform convulsions and attacks; defective reactions of the pupil; ptosis and ocular paralyses of all kinds; paralyses in the territory of other cranial nerves, such as the trigeminal and facial; paresis or paralysis of the lips, tongue, palate, and larynx; primary optic atrophy; ataxy and inco-ordination; tremor of various kinds; muscular atrophy, which appears as a rare manifestation in otherwise classical cases of tabes dorsalis; paresis of both cerebral and spinal origin; lateral sclerosis; various disturbances of sensation; visceral attacks, such as gastric crises; the most diverse conditions of the reflexes ranging in the case of the knee-jerks from exaggeration to complete abolition; sphincter affections and disturbances of the detrusor action of the bladder.

Now, it is only by arbitrary selection that these diverse signs and symptoms can be said to constitute two diseases. We shall attempt to show that they are all manifestations of a syphilitic state which can produce innumerable combinations of signs and symptoms, according to the parts which happen to be attacked. We shall also show that a patient, who at first developed one group of signs, may later exhibit other signs which, on the old nomenclature, would have carried him into another category.

Like all other syphilitic affections of the nervous system, "parasyphilis" is a widespread abnormal condition, and the clinical forms assumed by the disease depend solely on the parts attacked at the moment.

(a) Progressive Muscular Atrophy.

Dejerine [4] laid stress in 1889 on the frequent occurrence of muscular atrophy in tabes dorsalis, and attributed it to peripheral neuritis; he placed the incidence as high as 20 per cent. Although few would set the proportion as high, atrophy of spinal origin is a familiar complication of undoubted tabes dorsalis, and French authorities have long recognized it as a manifestation of parasyphilis (Kinnier Wilson [35]).

Fournier [9] insists that uncomplicated muscular atrophy may be parasyphilitic, basing his opinion on cases observed by Raymond [32], in one of which an autopsy was obtained. This revealed lesions of the spinal meninges, degeneration of the anterior roots, loss of cells in the anterior horns with profound endarteritis obliterans of the vessels. Raymond describes the condition as a vascular myelitis, showing nothing specific and resembling in no way the lesions of tertiary syphilis.

Fournier insists that these patients do not benefit even from the most drastic anti-syphilitic treatment, and points out that clinically the wasting is preceded by lancinating pains.

Mott [18] mentions that some forms of amyotrophic lateral sclerosis may be parasyphilitic, but cites no instances. Most German and English writers ascribe these cases to the direct action of syphilis, and do not consider the possibility that they may be parasyphilitic. Thus, Nonne [22] speaks of a meningomyelitis with participation of the anterior horns in the diffuse affection. He quotes amongst others both Raymond's and Dejerine's cases, but does not discuss their relation to parasyphilis.

On the other hand, A. Read Wilson [34] gathered together a series of cases of muscular atrophy, partly from the literature and partly from his own observation, in which the Wassermann reaction was positive in the serum, and classes them all as parasyphilis, oblivious of the extreme difficulty in differential diagnosis.

Now, there can be little doubt that in the majority of cases where syphilis is responsible for muscular atrophy, the condition is caused by a true syphilitic meningomyelitis. For not only are these patients

peculiarly susceptible to treatment with salvarsan or neo-salvarsan, but other signs are usually present pointing to a diffuse lesion of the spinal cord and its membranes. The following case is a good instance of muscular atrophy due to cervical meningomyelitis of syphilitic origin.

Case 36.—Rose C., aged 36. [Dr. F. J. Smith.] She was married in 1900, but left her husband three years later because he would not work. No definite history of infection could be obtained. She had never been pregnant.

In 1909 she suffered for four weeks from intense headache, which ultimately passed away entirely.

In December, 1910, she had a "stroke," her speech became affected, and she was unable to walk steadily. Since then her memory has deteriorated and she has been unable to work.

In January, 1912, her right hand began to waste, and she lost power so rapidly that, by June of the same year, she was unable to hold a knife. This wasting was thought at another hospital to be due to cervical ribs, and in July a rib was removed, but she steadily grew worse. In September the left hand became affected. Ever since the middle of 1912 she has been occasionally unable to control her motions and hold her water.

In November, 1912, she first came under our observation. Her speech was slurred and her memory defective. The pupils reacted to light, but the contraction was not maintained and tended to be rhythmic; on accommodation the reaction was normal. Her face was expressionless, and on the left side there was slight weakness of its lower half. The tongue moved well and was not tremulous. The fundi showed no abnormal appearances.

All the muscles of both hands, of both forearms, and to a less degree, of the arms, were considerably wasted, especially on the left side. The muscles of the shoulder-girdle were much less affected. Both lower extremities were slightly spastic.

No hyperalgesia or loss of sensation could be discovered, even in the arms. The knee-jerks were exaggerated; ankle-clonus was obtained on both sides and both plantar reflexes gave an extensor response.

She had considerable difficulty in holding her water and could not control her motions if they were soft.

The Wassermann reaction was:—

Serum	4.4.4.4.2.[1]
Cerebrospinal fluid	4.4.1.0.0.

[1] Throughout this investigation we record the results of the Wassermann reaction in this form. The test is quantitative and falling doses of serum and cerebrospinal fluid are used. Formerly we followed the usual method of recording the reaction and represented complete inhibition by + + + + and incomplete inhibition by + + +, + + or +. To economize space these would now be written 4, 3, 2, or 1. The figures 4.4.4.4.4 imply that the reaction was complete in each of the five dilutions, whilst 4.4.4.0.0 shows that the reaction was complete in the first three, but negative in the last two dilutions. Such results as 2.0.0.0.0 or 1.0.0.0.0 have no diagnostic value. The figures above the line always refer to the serum, those below the line to the cerebrospinal fluid.

But in the following case the picture was one of a typical muscular atrophy, complicated only by the defective reaction of the pupils.

Case 75.—William H., a married man, aged 36, began to lose power in the middle finger of his right hand two years ago (1911). About three months later wasting started in the left arm, and within the space of a year had progressed to such an extent that he was unable to use either arm.

On admission in March, 1913, all movements were impossible in the right upper extremity below the shoulder-joint, and all the muscles, especially those of the hand, showed intense wasting. He could slightly flex the ring finger of his left hand, and evoke a feeble contraction of the flexors of the elbow, but otherwise all muscular power was lost in the left arm. All movements of the right shoulder-girdle were lost; he could slightly contract the muscles of the left shoulder, but not with sufficient strength to produce any material change in the position of the limb. All the muscles of the neck were weaker than normal, and somewhat wasted.

The knee-jerks were brisk, ankle-jerks were easily obtained, and the plantar reflexes gave a flexor response.

He had suffered no pain, and no disturbance of sensibility could be discovered.

The pupils reacted extremely feebly to light, but reacted well to accommodation. The tongue showed no fibrillary tremor, and the movements of the palate and larynx were unaffected.

At no time had he experienced any trouble in holding or passing his water.

He was in the Army in 1896, and again between 1900 and 1908; but although exposed to infection, he can remember no venereal disease of any kind. But in spite of this complete absence of knowledge of infection, the Wassermann reaction was as follows:—

Serum	4.4.4.4.4.
Cerebrospinal fluid	4.4.4.0.0.

The cells were 44 per cubic millimetre.

Here, then, is a patient who differs from the usual cases of muscular atrophy due to syphilitic meningomyelitis in the absence of pains, of spastic signs, and in the integrity of the mechanism of micturition. At no time had there been any intercurrent manifestation which could be attributed to syphilitic vascular lesions in other parts of his nervous system.

On the other hand, this patient differed from a true case of progressive muscular atrophy in the defective reaction of the pupils, and in the presence of a positive Wassermann reaction in the cerebrospinal fluid; we are, therefore, inclined to believe that he is an example of parasyphilis amyotrophica. For had he been simply an instance of progressive muscular atrophy in a patient suffering from syphilis, the

reaction would have been negative and not positive in the cerebrospinal fluid.

(*b*) *Epileptic Manifestations.*

Fournier [10] called attention to a form of epilepsy, liable to appear many years after infection with syphilis, which was entirely refractory to antisyphilitic treatment. This, he believed, to be a manifestation of parasyphilis. He points out that syphilitic encephalopathy, accompanied by epileptiform convulsions, is characterized by the co-existence of other phenomena, pointing to a gross lesion of the brain, and rapidly produces other signs and symptoms indicative of cerebral syphilis. He insists that it runs its course with greater or less rapidity towards recovery or death, and that cerebral syphilis is peculiarly amenable to antisyphilitic treatment, even though complete recovery may not occur. But epilepsy of parasyphilitic origin tends to appear as an isolated symptom, and continues in this form without the addition or conjunction of other cerebral manifestations; it may last over a long period, and is refractory to antisyphilitic treatment; bromide does not produce a cure, but may moderate the frequency and severity of the attacks.

Nonne [23] entirely agrees with this description and accepts parasyphilitic epilepsy as a condition comparable to tabes dorsalis and dementia paralytica. He carefully differentiates it, on the one hand, from cerebral syphilis, and, on the other, from the seizures which may herald the early stages of dementia paralytica. It arises suddenly in later middle life, and continues for many years, resisting all antisyphilitic treatment.

The following case, where parasyphilitic epilepsy arose on a basis of congenital infection, illustrates the long duration of the disease, and is particularly interesting from the presence of Argyll-Robertson pupils.

Case 66.—Florence G., an unmarried woman, aged 24, has been under the care of H. H. for epileptiform attacks since September, 1904. In 1900, at the age of 11, she developed fits which have continued ever since, in spite of treatment. The attacks come on without warning, she passes water, falls, and has not infrequently hurt herself. Throughout she is completely unconscious and sleeps after the attack. Usually two or more fits occur in rapid succession.

Her memory and attention are poor, but she shows no gross signs of dementia. Her speech is unaffected, and, excepting after an attack, she is not liable to headaches or vomiting. She is somewhat deaf; the corneæ show

faint nebulæ, but the fundi are unaffected. The pupils are usually equal and of fair size, but they do not react to light: they react well to accommodation. Otherwise no affection can be discovered in the territory of the cranial nerves. The knee-jerks and other reflexes, including the plantars, are normal, except after a series of convulsions. Motion, sensation, and the action of the sphincters are entirely unaffected.

She is short and broad, 4 ft. 10 in. (146 cm.) in height, with a narrow forehead and pegged teeth. Scars are visible at the angles of the mouth, and she has the appearance of a case of congenital syphilis.

In June, 1913, the Wassermann reaction was as follows:—

Serum	4.4.2.0.0.
Cerebrospinal fluid	4.4.4.4.0.

The cells were 40 per cubic millimetre.

Such reactions are incompatible with the diagnosis of uncomplicated congenital syphilis and point definitely to infection of the central nervous system. At the same time there are no signs of any affection of the meninges or spinal cord, and we believe this patient is an instance of parasyphilitic epilepsy.

(*c*) *Lateral and Combined Sclerosis. (Erb's Syphilitic Spinal Paralysis.)*

An incomplete transverse myelitis is universally recognized to be the commonest form of syphilitic disease of the spinal cord. This myelitis is a diffuse inflammatory and vascular disturbance, bearing all the marks of a direct hyperplastic reaction to the infection.

But in 1892 Erb [6] suggested that syphilis might produce degeneration of the long paths, such as the pyramidal tracts, not as a consequence of interruption by inflammatory foci, but as a direct effect exercised by the poison upon them. For many years doubt has been thrown on the existence of such tract degenerations, in consequence of the extreme difficulty in differentiating clinically between the results of a diffuse meningomyelitis and those produced by primary degeneration of the posterior and lateral columns of the cord. In both cases the signs may consist solely of increased knee-jerks, ankle-clonus with extensor plantar reflexes, more or less spasticity, and ataxy, with loss of recognition of posture and passive movement in the lower extremities.

However, there can now be little doubt that primary degeneration of the lateral, with or without degeneration of the posterior columns, may occur as a consequence of syphilitic infection. Nonne [24] sums up an admirable discussion of the question in the following conclusions: (1) It is certain that cases exist which show exactly the signs and

symptoms described by Erb; (2) this disease may be caused by several anatomically distinct conditions. It may be due to a true combined degeneration or to a degeneration of the long tracts caused by a chronic myelitis or meningomyelitis with more or less vascular disease.

Meanwhile, the idea was growing up that possibly Erb's spinal paralysis might be of parasyphilitic origin. But, in view of the extreme difficulty in making a differential diagnosis during life, this view remained a tentative suggestion.

We believe that these cases of lateral or combined sclerosis, however closely they may resemble one another clinically, may be based pathologically either on syphilitic inflammation or so-called "parasyphilitic" degeneration. More commonly, they are the expression of tertiary meningeal and vascular changes; under these circumstances they will probably respond to antisyphilitic treatment, and at the same time the Wassermann reaction in the cerebrospinal fluid will rapidly diminish and may even become negative. A large number of these patients with late meningomyelitis at one time or another show signs of some root-lesion; these signs, although of extreme differential importance in diagnosis, not uncommonly pass unobserved, as they do not obtrude themselves on the patient's consciousness. We believe that the following case is an example of this condition:—

Case 91.—Dennis K., labourer, aged 36. In 1904 he contracted syphilis and suffered from a chancre, rash, and sore throat, for which he was treated with mercury by the mouth for twelve months.

In 1907 he developed gummatous ulcers on his shins, which healed rapidly under the administration of iodides.

On January 4, 1912, he was taken ill with dizziness, pains in his belly, and repeated vomiting. This attack was followed by headache which lasted till his admission in July, 1912.

About four weeks before admission, a pimple appeared on his palate which enlarged, broke down, and led to a perforation into the nose.

On admission (July, 1912), his mental state was unaffected, but he suffered from severe headache. The knee-jerks were brisk and both plantars gave an extensor response. He walked well and was not ataxic, but both great toes tended to remain in the extended position. There was no loss of muscular power.

Distinct hyperalgesia was present in the region of the eighth and ninth thoracic roots on both sides, but no sensory change could be discovered elsewhere to any test. The pupils reacted well, and the movements of the face, tongue and palate were normal. He had a little difficulty in beginning micturition, but no other sphincter trouble.

The Wassermann reaction was :—

Serum	4.4.3.0.0.
Cerebrospinal fluid	4.4.4.1.0.

He was given 0·6 grm. of salvarsan intravenously on July 10, 1912, and a similar dose on the 17th. By January 15, 1913, the reaction had become :—

Serum	3.2.1.0.0.
Cerebrospinal fluid	1.0.0.0.0.

At the same time the headache and hyperalgesia around the trunk disappeared and his general condition improved strikingly.

This is a characteristic instance of degeneration of the lateral columns of the cord, depending on a chronic meningomyelitis.

Compare with this case the following one, which we believe to be an instance of parasyphilis.

Case 71.—William H., labourer, aged 54. He denies all infection with syphilis, but in 1875, at the age of 17, and again in 1878, aged 20, suffered from gonorrhœa. Neither attack was accompanied by a sore, rash, or other secondary manifestation of syphilis.

In 1907, his eyesight began to fail, and in 1910, his legs became stiff and his gait unsteady.

When admitted to the hospital in February, 1912, his mental state was normal, his speech unaffected, and he had not suffered from fits or any other attacks.

His gait was spastic, but there was no paralysis or loss of muscular strength. He tended to sway slightly with his eyes closed, but did not fall.

The knee-jerks were exaggerated, ankle-clonus was obtained, and the plantar reflex gave an extensor response on both sides.

There was no gross loss of recognition of posture and passive movement, and he responded well to the tuning fork tests. Sensation to touch, pain, heat and cold was entirely unaffected.

Both pupils reacted readily to light and accommodation in spite of his defective vision.

Vision in both eyes was very poor, and the letters of the test types could not be distinguished at six metres. The discs were pale with a distinct lamina cribrosa and clear edges.

No other special senses were affected.

Face, tongue, and palate moved normally.

He had difficulty in passing his urine, and on admission, he was suffering from overflow from a distended bladder.

The Wassermann reaction was :—

Serum	4.3.2.0.0.
Cerebrospinal fluid	4.4.4.3.0.

Cells were 12 per cubic millimetre.

The contrast between these two cases is striking. In D. K. (Case 91) the infection was definite and was followed by undoubted secondary manifestations; twelve years later he developed a gumma of the palate with headache, signs of lateral sclerosis and of an irritative lesion of thoracic nerve-roots. He improved greatly under salvarsan, and the Wassermann reaction in the cerebrospinal fluid fell rapidly. In fact he was a typical instance of tertiary meningomyelitis.

In W. H. (Case 71), on the other hand, the infection was doubtful, and, as in so many cases of tabes dorsalis, was followed by no secondary manifestations. The whole infection ran its course under cover of a gonorrhœa. Nearly thirty years later, he first began to lose his sight from primary optic atrophy, and a little later developed the signs of lateral sclerosis. The Wassermann reaction was positive in serum and cerebrospinal fluid.

(*d*) *Optic Atrophy.*

In the consideration of primary optic atrophy, we are faced by exactly the opposite problem to that in the case of the primary tract degenerations. It appears so frequently as an accompaniment to tabes dorsalis that its parasyphilitic origin is universally acknowledged, even when it occurs alone. Thus Nonne [25] goes so far as to say that primary optic atrophy is almost always a manifestation of tabes dorsalis, and not infrequently may exist alone for a long period before the appearance of other signs of the disease.

Yet he gives [26] a perfect instance of a woman whom he had watched for eighteen years with primary optic atrophy, and no signs of tabes dorsalis or dementia paralytica had so far appeared.

Case 186.—Jane A., a widow, aged 60. In 1875, at the age of 22, she married her first husband, who died six years later from asthma and bronchitis: two out of three children, the issue of this marriage, are alive and well. In 1892 she was married again to a husband who ultimately developed dementia paralytica and died insane in 1912. In this marriage she had two children, the first of whom, born in 1893, died of wasting at three months old, whilst the second, born two years later, is living and healthy.

In 1905 she began to suffer from pains in the chest, but in view of the large gastric ulcer from which she ultimately died, these pains are of doubtful significance.

In 1907 she began to lose her eyesight. This loss of vision progressed slowly and culminated in 1910 in complete blindness.

When admitted in May, 1913, she was a sallow, anæmic woman, extremely

intelligent, but totally blind. She suffered mainly from hæmatemesis and malæna, which were due to a large chronic ulcer of the stomach.

She showed no loss of memory or attention, and had had no seizures or fits of any kind.

Her speech was unaffected.

There was no tremor, no ataxy, and she did not become unsteady when her eyes were closed. No loss of sensation could be discovered to touch, pain, or temperature, and she was able to appreciate perfectly the vibrations of a tuning fork. Recognition of posture and passive movements was unaffected.

The knee-jerks and ankle-jerks were normal, and both plantar reflexes gave a flexor response.

She was completely blind and the discs were in a condition of primary white atrophy. Hearing, smell and taste were unaffected. The pupils were equal and reacted well to accommodation. They did not react to light in consequence of her blindness. All movements of the eyes, face, tongue, palate, and larynx were performed normally. The sphincters were unaffected.

The Wassermann reaction was:—

Serum	4.4.3.0.0.
Cerebrospinal fluid	4.4.3.0.0.

The cells were 30 per cubic millimetre.

She died suddenly on May 30, 1913, of hæmatemesis, and at the *post-mortem* examination, a large chronic ulcer of the stomach was found, which had opened one of the coronal arteries. The brain and spinal cord showed no signs of gummatous meningitis, and we believe that she was a case of parasyphilis optica.[1]

We have already described a case of parasyphilitic lateral sclerosis with primary optic atrophy (Case 71, p. 10), and it will, perhaps, be worth quoting an instance of optic atrophy with loss of knee-jerks, observed over a period of ten years.

Case 131.—Edward R., aged 52. In 1885, at the age of 24, he developed a chancre, followed by a rash and a sore throat. He was treated for six weeks only, but remained in perfect health.

In 1895, at the age of 34, he went blind from primary optic atrophy, and has been under the care of H.H. for the last ten years. From the beginning, his knee-jerks and ankle-jerks have been absent, but he has shown no signs of ataxy, tremor, or defects of speech. We have never been able to discover any disturbance of sensation.

In August, 1911, he had a sudden attack of confusion with loss of memory, which passed away and left him in his previous condition. With this exception he has not progressed, and is in the same state in which he was first seen ten years ago.

[1] A complete account of the *post-mortem* examination will be published later.

The Wassermann reaction in September, 1911 was :—

Serum	4.4.2.1.0.
Cerebrospinal fluid	4.4.4.3.1.

and the cells were in excess.

Similar cases occur repeatedly in the literature and there can be no difference in principle between them and the rare instances where the knee-jerks and other deep reflexes happen to be normal.

No one can therefore doubt that primary optic atrophy can occur as a parasyphilitic phenomenon, alone, or in combination with primary degeneration of the lateral or posterior columns of the spinal cord.

(2) *Clinical Antecedents.*

The first essential factor in the development of parasyphilis seems to be time. In many cases, where the affection of the nervous system is a manifestation of active syphilitic changes, the first symptoms occur within ten years of infection. An analysis [13] of 33 cases in males, where the date of infection was known, showed an average of two years and eight months.

On the other hand, in 38 cases of tabes dorsalis seen by H. H. in private practice, where the date of infection could be determined accurately, the first symptom, usually consisting of pains, appeared on an average after an interval of fourteen years. The average of 11 hospital cases in males, observed by ourselves, where the signs of disease were characteristic and the Wassermann reaction was strongly positive in the cerebrospinal fluid, also gave an average period of fourteen years.

Secondly, in a large proportion of cases of parasyphilis, the primary and secondary manifestations have been extremely slight. Thus, out of 40 undoubted cases of tabes dorsalis seen in private practice, all infection with syphilis or gonorrhœa was denied in 3[1]; gonorrhœa only had existed in 9, whilst 13 had suffered from a chancre without any secondary manifestations. All of these 13 patients were under careful medical treatment, and it is unlikely that a rash, sore throat or fall of hair would have escaped observation. Thus, out of 40 cases of tabes dorsalis 25, or 62 per cent., showed at most a primary sore in consequence of infection.

Amongst 15 hospital patients with tabes dorsalis in whom the Wassermann reaction was strongly positive, both in the serum and cerebrospinal fluid, 3 denied all venereal disease, but acknowledged

[1] One of these patients had lived with a woman who developed syphilis. He was carefully examined at the time by experts who could find no trace of any venereal disease in him.

frequent exposure; one had suffered from gonorrhœa only, whilst in 5 a chancre had been present followed by no secondary manifestations. Here again in 60 per cent. a primary sore had been the maximum consequence of infection.

The third peculiarity, which is revealed by the study of cases of undoubted parasyphilis, is the apparent want of correspondence between the efficiency of the treatment in the early stages of syphilis and the appearance of parasyphilitic disease. Many of the men seen in private practice had been treated by the highest authorities in this country and abroad; mercury may have been given by the mouth for three or even more years, they may have been to Aachen year after year, and yet tabes dorsalis appeared, exactly as in the hospital patient who had at most "taken medicine" for a few weeks. Moreover, the form of the disease and the frequency of its occurrence does not vary materially in the different European countries amongst those who have been exposed to infection, in spite of the diverse methods of treatment in vogue.

Chapter II.—The Wassermann Reaction.

(1) *In Syphilis and Parasyphilis of the Central Nervous System.*

With the discovery by Wassermann and Plaut [33] that the cerebrospinal fluid reacted positively in cases of dementia paralytica, a problem was stated, to which the answer is still uncertain. Innumerable examinations have been made and columns of statistics compiled by laboratory workers who knew little or nothing of the source of the fluid they were investigating, beyond the diagnosis of the disease; in many cases the cerebrospinal fluid had even been sent from hospitals or asylums at a distance. But, as Plaut [29] himself points out, the difficulties in differential diagnosis, particularly between active syphilitic disease of the brain and parasyphilis cerebralis, are often extreme; one falsely diagnosed case of this kind may ruin a column of statistics, and we believe that want of accuracy and fulness in the clinical examinations of patients, from whom serum and cerebrospinal fluid has been withdrawn, is responsible for much of the confusion which exists at present. The time for collecting mass statistics is over, and each case must be investigated with as much care as if it were to be published separately. This we have attempted to do; we have included no case that has not been examined by one of us and where every note has not been taken by ourselves.

The form of the Wassermann reaction we have employed has been evolved during the last five years in the course of general diagnostic work in several thousand cases of all forms of disease. It differs from the so-called "original method," as finally described in 1913 by Plaut [30], in the following particulars:—

(*a*) The fixation stage is carried out with more concentrated constituents.

(*b*) The cerebrospinal fluid is used in greater quantity and *unheated*. Thus we use 0·2 c.c. of the fluid in 1 c.c. during the fixation stage of the reaction, while the "original method" employed 0·2 c.c. of *heated* cerebrospinal fluid in 3 c.c. In the so-called "Auswertungsmethode" 1 c.c. of cerebrospinal fluid is used in 3 c.c.

(*c*) A heart cholesterin antigen is used [16].

(*d*) The complement is standardized against a constant quantity of amboceptor.

(*e*) Every case is tested quantitatively by titration of the serum and cerebrospinal fluid.

During the last fifteen months we have examined by this method 372 cases where the diagnosis of syphilitic infection was made by Dr. J. H. Sequeira, and verified by continuous observation of the patients. The results were as follows:—

Primary syphilis	...	...	93	per cent.	positive.
Secondary ,,	...	...	99	,,	,,
Tertiary ,,	...	...	97	,,	,,
Congenital ,,	...	...	100	,,	,,

Only one apparently non-syphilitic individual gave a positive reaction, a case of acute malaria twenty-four hours after the rigor.

As a control on the method employed, we investigated thirty-two cases of gross nervous disease in patients in whom there was no reason to suspect the presence of syphilis, and did not find a single instance in which either blood or cerebrospinal fluid reacted positively. These included eight cases of cerebral tumour; five cases of vascular lesions of the brain, such as embolism, thrombosis, and hæmorrhage; five cases of disseminated sclerosis, two cases of spinal tumour, three cases of other chronic spinal cord conditions, three cases of peripheral neuritis, and three cases of neurasthenia.

As a further control of our clinical observations we examined twenty cases of undoubted syphilis, without obvious signs pointing to affection of the central nervous system. In every case the serum was positive and the cerebrospinal fluid negative. At the same time we have

observed a certain amount of delay in the hæmolysis of the cerebrospinal fluids of patients with secondary syphilis, and in view of the results of Altmann and Dreyfus [1], and Max Fraenkel [11], we accept the occasional occurrence of a positive reaction in the cerebrospinal fluid of patients with secondary syphilis.

The serological results obtained by us in cases of gross disease of the central nervous system of syphilitic origin can be tabulated shortly as follows:—

	Number of cases	Positive reaction in	
		Serum	Cerebrospinal fluid
Dementia paralytica and tabo-paresis ..	17 ..	17 ..	17
Tabes dorsalis	24 ..	20 ..	22
Cerebrospinal syphilis—			
(*a*) With involvement of the spinal cord ..	23 ..	22 ..	21
(*b*) Without involvement of the spinal cord	25 ..	22 ..	7

Now it is obvious that these results agree in some respects with those of previous workers, whilst in other directions they differ fundamentally.

In dementia paralytica our figures correspond with those published in the literature, although the number is too small to disclose the rare occurrence of negative reactions in the cerebrospinal fluid. Among the twenty-four cases of tabes dorsalis, two gave a negative reaction in the cerebrospinal fluid; both these patients were in a completely stationary condition. Thus, in tabes dorsalis the reaction may be diminished or lost in consequence of fluctuations in the activity of the disease, a factor which is not present as far as we know in dementia paralytica.

Such diminished activity may be due either to the long period during which the disease has lasted, or perhaps occasionally to the severity of the anti-syphilitic treatment.

In progressive cases the reaction is almost uniformly positive, both in the serum and cerebrospinal fluid.

Although the strength of the reaction is usually less in comparison with that found in dementia paralytica, nevertheless in the cerebrospinal fluid of patients with tabes dorsalis, it is often very strong and little reliance can be placed upon the strength of the reaction for the purposes of differential diagnosis.

When we turn to the results obtained by us in cerebrospinal syphilis, they differ considerably from those recorded in the literature.

According to Plaut [31] "Sowohl bei Lues cerebri als bei Lues spinalis ist die negative W. Reaktion des Liquor die Regel. . . .

Dieses Verhalten findet sich in gleicher Weise bei allen Formen der Erkrankung. . . ."

Nonne [27] gives as a typical result in the fluid of cerebrospinal syphilis:—

"(*a*) Originalmethode (0·2 c.c.) positiv in ca. 10. Proz.

"(*b*) Höhere Liquormengen fast stets positiv."

This remark dealing with the quantity of test fluid refers to the "Auswertungs-Methode" of Hauptmann and Hössli [12], according to which five times the ordinary quantity of cerebrospinal fluid is used. This method gives a much larger number of positive reactions than the "original method," especially in cerebrospinal syphilis, but the majority of these positive results are obtained with the larger quantities of fluid only; thus it is clear that in Nonne's view the strength of the reaction in cerebrospinal syphilis is slight. He says [27] "Ist die Wassermannsche Reaktion schon nach der Originalmethode (0·2 c.c. des zu untersuchenden Liquors) positiv"—that is if the reaction is strong—"so besteht die grosse Wahrscheinlichkeit, dass es sich bei dem vorliegenden Fall um eine Paralyse oder Taboparalyse handelt, weit seltener um eine Lues cerebrospinalis oder um eine reine Tabes."

However, as will be seen from our figures, this view appears to be untenable. We have formed the opinion that there is a great difference between cases of syphilis of the central nervous system according to whether the spinal cord itself is affected or not. This difference is found both in the incidence of the reaction and in its strength. We have found that in "spinal" cases the reaction is not only constant in the cerebrospinal fluid but also strong, certainly as strong as that found in dementia paralytica. In "cerebral" cases, on the other hand, the reaction is much less constant and is quantitatively weak. We therefore dispute the suggestion, that either the occurrence of the reaction in the fluid or its strength has an obvious bearing upon the differential diagnosis between dementia paralytica and cerebrospinal syphilis.

As has already been pointed out by Assmann [2] and by Plaut, the purely endarterial forms of cerebral syphilis tend to give negative reactions in the cerebrospinal fluid more frequently than the meningeal. We have also further observed that a positive reaction in the purely cerebral forms is more frequent, though feeble, when the test is applied shortly after the onset of the symptoms.

The great outstanding difference between the reaction in "parasyphilis" and cerebrospinal syphilis is the prompt effect of antisyphilitic treatment upon the latter condition. The strong reaction

in the cerebrospinal fluid of a case of meningomyelitis may be rapidly reduced or made negative by salvarsan injections, while the same treatment appears to have much less effect, if any, in dementia paralytica, and very little in tabes dorsalis. It is therefore absolutely essential in every case to determine the amount of treatment to which the patient has been subjected before a serological investigation is interpreted.

As an example of the different behaviour of the Wassermann reaction under treatment in syphilis and parasyphilis, we may instance the following cases:—

Chronic Spinal Meningitis (*Case 91*)—

	Serum	Cerebrospinal fluid
July 10, 1912	4.4.3.0.0.	4.4.4.1.0.
Two doses (0·6 grm.) of salvarsan.		
January 15, 1913	3.2.1.0.0.	1.0.0.0.0.

Tabes Dorsalis (*Case 37*)—

	Serum	Cerebrospinal fluid
October 8, 1912	4.4.2.0.0.	4.4.3.1.0.
Two doses (0·9 grm.) of neo-salvarsan.		
May 7, 1913	4.4.4.2.0.	4.4.2.0.0.

We may summarize our results as follows:—

In dementia paralytica and tabo-paresis a strong reaction is almost constant in both serum and cerebrospinal fluid. The presence of a negative reaction would make a diagnosis of these conditions highly improbable.

In tabes dorsalis the reaction is almost constantly positive in serum and cerebrospinal fluid, except when the activity of the disease has subsided as a result of time or treatment. The strength of the reaction is often not so great as that in dementia paralytica; on the other hand, this is in no way a constant rule. Thus, a negative reaction obtained during an active stage of a suspected case of tabes dorsalis would render the diagnosis unlikely.

In untreated cerebrospinal syphilis, the reaction in the spinal fluid varies according to the site of the lesion. When the spinal cord and its meninges are affected, the reaction is positive and usually very strong; but when the signs indicate that the cord has escaped, it is inconstant, and, when present, weak. The reaction is most often positive when the lesions are recent. In treated cases, the reaction is positive in the cerebrospinal fluid according to the efficiency or otherwise of the treatment.

(2) *The Origin of the Wassermann Reaction in the Cerebrospinal Fluid.*

In order to discuss the origin of this reaction and its behaviour under various conditions, it will be necessary to consider the researches of Turnbull upon the subarachnoid space and the deductions drawn therefrom by Fildes. These views differ considerably from those usually taught.

We believe that the subarachnoid space is a closed cavity, potential in the cranium and actual in the spinal canal. It is filled with a relatively stagnant cerebrospinal fluid, which acts simply as a water cushion to the spinal cord and brain-stem.

The cerebrospinal fluid serves no lymphatic function and is shut off from the lymphatics of the brain, cord and roots by the endothelium covering the walls of its containing space.

The origin of the cerebrospinal fluid is unknown; but in all probability it is a secretion of the endothelium lining the subarachnoid space. It is doubtful to what extent the ventricular fluid contributes to its constitution, and we think it is improbable that this fluid passes directly from the ventricles into the cerebrospinal fluid by way of the foramen of Magendie, even when this exists. Normally the cerebrospinal fluid in the cranium is a mere film of moisture lubricating the opposing walls of the subarachnoid space as in a joint cavity; in the spinal canal it collects in some bulk and remains in a relatively stagnant condition. Under abnormal circumstances the quantity of fluid may be increased, and, when degenerative or inflammatory conditions of the pia are present, unusual substances may contaminate it as an exudate. Even when the pia is unaffected, such substances as the endothelium is capable of secreting may find their way into the fluid.

The Wassermann substance is not capable of passing an intact membrane, and it will only appear in the spinal fluid when the pial covering is diseased. The source of the Wassermann substance throughout the body is a syphilitic focus; it probably represents one of the elements derived from a cell which has been specifically affected by the *Spirochæta pallida*. Its source, therefore, in the central nervous system will be either a meningeal and vascular focus in cerebral syphilis or a "parasyphilitic" focus in parasyphilis. An acute or chronic meningitis will obviously involve the pia mater, and the products of this process, including the Wassermann substance, will pass into the cerebrospinal fluid; thereaction will therefore be positive. If, however, the lesion is purely thrombotic, and the meninges are little affected, the

Wassermann substance will not pass into the fluid to any great extent. The reaction in the cerebrospinal fluid may therefore be negative or slightly positive only. Further, it must be remembered that the test fluid is collected from a site far distant from the brain and that, if there is any interruption to a free passage of the fluid from the brain to the spinal cord, Wassermann bodies, poured into the cerebral subarachnoid space, may not reach the lumbar region. In this manner we endeavour to explain the fact, that in a purely cerebral lesion, whether meningeal or not, the cerebrospinal fluid usually yields a negative reaction, while, when the cord is affected, it is positive. Now a gummatous process is known to be peculiarly susceptible to salvarsan treatment; such a lesion therefore may be rapidly healed and the pia reduced to a normal condition. That is to say, both the source of the Wassermann bodies and the opportunity for their entry into the fluid may be readily abolished. In such cases, therefore, the Wassermann reaction should rapidly become negative in the fluid, and this we have shown to be the case (*vide* pp. 10 and 18.)

Turning to the consideration of parasyphilis, we hold that the origin of the reacting substance is the "parasyphilitic" lesion which, as we show later, is situated in the nervous tissue. This substance does not find its way into the fluid by means of any of the "normal" channels which have been described, but passes up the adventitial lymphatics to the pia. This pial membrane is always diseased in dementia paralytica and tabes dorsalis, and thus the reacting substance can pass into the cerebrospinal fluid. But this Wassermann reaction cannot be made negative by treatment under ordinary conditions, because antisyphilitic remedies circulating in the blood-stream cannot obtain access to those essential tissues of the central nervous system, which form the "parasyphilitic" focus (*vide infra*, p. 27). The process will therefore continue unhindered to give rise to the substance responsible for a positive Wassermann reaction in the cerebrospinal fluid.

Chapter III.—A Theory of Parasyphilis.

(1) *The Pathological Anatomy of Parasyphilis.*

Parasyphilis of the nervous system is a widespread condition, which may affect every structure in the brain and spinal cord. If we wish to study the anatomical changes with which it is associated, it is useless to examine long-standing cases of such a disease as tabes

dorsalis; the essential lesions have long given place to chronic conditions, which reveal little of the nature of the original reaction. But a study of the spinal cord in cases of tabo-paresis, where the patient has been killed by the cerebral lesions, at a time when those in the spinal cord are still fresh, throws more light on the nature of the fundamental processes.

According to the views widely adopted at the present time, parasyphilis of the nervous system depends on an atrophy of the nerve-fibres and cells, associated with a cellular infiltration of the meninges and adventitial sheaths of the vessels and proliferation of the neuroglia. The majority of the authorities look upon the degeneration of the essential nervous structures as primary, and the vascular and glial proliferation as a secondary sclerosis. Some, however, have urged that, at any rate in tabes dorsalis, the degeneration is secondary to changes in the meninges and adventitial sheaths of the vessels.

On the other hand, the lesion of chronic syphilitic meningitis (gummatosis) appears to be of a different nature; it starts as a lymphocytic accumulation about a small vessel, the lumen of which tends to become obliterated by proliferation of its endothelium. The accumulation of plasma cells and fibroblasts then leads to the formation of a definite granuloma. Any degeneration of nerve-fibres or cells which may occur is produced by interference with the blood-supply or pressure of the inflammatory tissue.

We have elaborated the view that, in all the lesions of active syphilis, the interstitial reaction is the same in quality, and differs only in the relative number of the reacting cells. Everywhere the activity of the spirochæte is manifested about itself as it lies in the neighbourhood of a capillary. There occurs a reaction of the fixed cells and a reaction of the wandering cells, producing a localized collection, or series of collections of lymphocytes, and later of plasma cells and fibroblasts. The same sequence is discoverable in chancres, papules and gummata, and the gross appearance of the lesion is dependent merely upon the amount of thrombosis and fibrosis. In those organs which contain a specialized parenchyma, a reaction may also occur in these cells, and the result will be degeneration followed by more or less recovery; the amount of this recovery will depend on the extent to which these specialized cells possess the power of regeneration.

The differences between the microscopical anatomy of the changes which occur in chronic syphilitic meningitis and in "parasyphilis," are generally supposed to represent a fundamental difference in the nature

of the pathological process. Nevertheless, in our view there is no such essential difference between the two conditions from a pathological aspect. We look upon a "parasyphilitic" lesion as a reaction and not as a degeneration; it is a reaction to the same toxic influence, the *Spirochæta pallida*, as that which evokes a gumma. But in the one case the chief reaction occurs in the nerve-cells (parenchyma of the brain) and neuroglia, whilst in the other the chief reaction occurs in the meninges and vessels (interstitial tissues of the brain). Parasyphilis of the brain or cord therefore corresponds to the parenchymatous lesions of the testicle (so-called parasyphilis of the testicle), while the gummatous lesions of the brain correspond to gummatous (interstitial) orchitis.

When a spirochæte, as shown by Noguchi [21], appears in the nervous tissues, there is a double reaction: firstly of the nerve-cells (parenchyma) and neuroglia (fixed interstitial cells); and secondly, of the wandering cells. These latter may be observed in large numbers, lymphocytes and plasma cells, filling the lymph spaces of the meninges and perivascular sheaths; but they are largely prevented from reaching the actual site of the spirochæte by the peculiar anatomical configuration of the part. They lie within the adventitial sheath of the vessels and are excluded from the nerve-tissues proper by this sheath, which is a continuous uninterrupted boundary, an extension of the limiting membrane of Lenhossek, between the nerve-tissues and the vessels. Thus, although the fixed elements, nerve-cells and neuroglia will react locally, the wandering cells remain distant and diffuse, and no "gumma" will be formed. As regards the nerve-cell itself, the reaction must entail a certain amount of death and degeneration.

Thus, a "parasyphilitic" disease is not due to a simple degeneration of nerve-elements, but is a reaction, affecting all the tissues which lie within the brain and spinal cord, and does not differ in pathological essentials from the reaction in chronic syphilitic meningitis. What then is the essential nature of a reaction which can manifest itself in such various anatomical changes as "gummatosis" and "parasyphilitic" disease?

(2) *The Nature of the Toxic Action in Parasyphilis.*

Mott [19] believes that this condition is in the strictest sense a non-specific sequel to syphilitic infection; the nerve-elements have reacted over a long period to the poison, and, in the attempt, fall victims to exhaustion and early death. The changes in neuroglia and lymphatic

channels are consequent on the necrosis of the cells and fibres and are a secondary expression of the same toxic activity.

The remarkable tendency of some strains of syphilis to infect the nervous system led many, especially the French authorities, to postulate a "Syphilis à virus nerveux." With the final recognition that tabes dorsalis and dementia paralytica demanded syphilis as an antecedent condition, the discussion as to the existence of a nerve-poison in some brands of infection shifted somewhat. Investigators began to suggest that some syphilitic infections might carry with them a peculiar liability to evoke parasyphilitic disease, and the notorious tendency of tabes dorsalis to follow mild primary manifestations was used as an additional support to this supposition. Cases were described [17] where one woman infected several men, all of whom developed parasyphilis; and Brosius [3] placed on record the story of seven glass-blowers who caught the disease from the same fellow workman; four out of five, who were examined twelve years later, were affected with nervous disease thought to be parasyphilitic.

Neisser [20] pays little attention to the question of parasyphilis but says: "Es kann wohl kein Zweifel darüber bestehen, dass, in der Pathogenese dieser Krankheiten die Syphilis zwar das wichtigste, ja sogar wohl unerlässliche ursächliche Moment darstellt, aber nicht das einzige. Sicherlich gehören entweder bestimmte ererbte Prädispositionen, oder bestimmte anderweitige Schädigungen (Alkohol) dazu, um bei Syphilitikern Tabes und Paralyse zu erzeugen, falls man nicht die Hypothese, dass es ein spezifisches Nervenvirus gibt, akzeptieren will." Thus it is obvious that, although he accepted tertiary manifestations as a striking evidence of the extent to which the mode of reaction of the tissues had been changed ("Umstimmung"), he did not think that it bore materially on the phenomena of parasyphilis.

With von Pirquet's conception of "allergie," a line of thought was opened which led McIntosh and Fildes to formulate the view we hold with regard to the nature of parasyphilis. Von Pirquet showed that all infections led to a change in the character of the reaction of the tissues to the poison. This might take place in two directions; they might respond less and less to infection ("hypoallergie"), until at last they ceased to respond altogether and became "anergic." But, on the other hand, a change in the opposite direction might occur; the reaction might appear both more quickly and with greater violence to a smaller dose of the poison. This he spoke of as "hyperallergie" and brought into this category the phenomena, described by Richet, under the name of "anaphylaxis."

Von Pirquet had no opportunity of working on the manifestations of syphilis in the light of this conception, but he quotes Finger and Landsteiner as showing that the period of incubation of a second infection can be shortened, and that patients with tertiary syphilis may react locally to the injection of syphilitic material.

In our view tertiary and "parasyphilitic" phenomena are manifestations of hypersensitiveness ("hyperallergie"), which reaches its extreme form in anaphylactic shock. As the tissues are hypersensitive, they react more strongly to a minute dose of the poison, and hence some of the difficulty of discovering the spirochæte in gummatous and parasyphilitic tissues.

The difference between the anatomical consequences, produced by the impact of the poison in the two cases, depends on the nature of the tissue attacked. Thus, gummatosis is the reaction of hypersensitive vessels and connective tissue, parts which tend to show proliferative changes. On the other hand, the pathological anatomy of "parasyphilis" of the central nervous system is the expression of the response of hypersensitized, highly differentiated nerve-elements which have no power of regeneration. The profound difference between the two forms of disease-process depends, not on the extent to which the tissues have become hyperallergic, but on the fact that, in the one case, proliferative repair can occur at once, whilst, on the other hand, the injury to the nerve-elements results in their death. This view explains the fact that "parasyphilitic" processes occur in those nerve-fibres in which the sheath of Schwann is absent. This structure is not only an essential factor in the process of regeneration, but also, no doubt assumes a nutritive or protective rôle, to such an extent that a reaction which is sufficient to destroy a nerve-fibre not provided with this sheath may be insufficient to injure to any considerable extent the nerve protected by the neurilemma.

This theory also accounts for the occasional presence in the same patient both of gummatous meningitis and of "parasyphilitic" degeneration; the one is the reaction of a highly sensitized connective tissue, whilst the tabetic changes are the expression of a similar condition in the long fibres of the posterior columns.

On this view we can also explain the peculiar course of the milder forms of parasyphilis. The tendency of many cases of tabes dorsalis is to run on somewhat acutely to a certain stage and then to stop, frequently for many years. This is particularly well seen where the first manifestation takes the form of primary optic atrophy, which leads invariably

to complete blindness; but from that time onwards the patient may remain free from any further affection until, perhaps many years later, his knee-jerks disappear, or he suffers from some cerebral complication.

(3) *How is the Central Nervous System rendered Hypersensitive to the Spirochæte?*

In order that a part of the body may be rendered hypersensitive, it must have been exposed previously to the influence of the toxic agent. Thus, a patient who has had tuberculosis may be rendered so hypersensitive to the organism that minute and otherwise harmless doses, even of tuberculin, applied at a later date, will produce an immediate reaction. In the same way, the tissues of a syphilitic patient become hypersensitive, so that a reapplication of the virus from without or the recrudescence of spirochætes within, will produce a large reactive lesion (syphilitic pseudo-chancre, gumma) out of all proportion to the number of spirochætes present. The central nervous system, also, may be sensitized, and the reappearance of spirochætes at a later date then produces an exaggerated reaction either in the nerve-tissues proper or in the vascular tissues of the nervous system. How then can this sensitization of the central nervous system be brought about under the influence of syphilitic infection?

According to the extensive researches of Orr and Rows [28], the perineural lymphatic space, which surrounds every spinal nerve and extends along the roots to the pia mater, is the afferent lymphatic channel of the central nervous system, while, according to Turnbull, the lymph spaces of the pia, which are in connection with these perineural sheaths, are also direct continuations of the adventitial lymph spaces of the perforating vessels. Thus we hold the view, that the space within the adventitial sheath of the finest capillary is in direct continuity, by means of lymph spaces, with the lymphatics of the spinal nerves, and that substances, ascending such nerves (Orr and Rows), will be brought into intimate relation with the nerve-tissues of the central nervous system.

Further, both Ehrmann [5] and Levaditi [14] have shown that the *Spirochæta pallida* may pass from a primary sore up the peripheral nerves; they discovered the organism not only in the lymph spaces of the perineurium, but actually between the nerve-fibres. It may, therefore, be assumed that the *Spirochæta pallida* is equally capable of affecting the cutaneous nerves during the secondary period, and hence the

central nervous system, especially that part related to the afferent peripheral nerves (posterior roots), will come under the influence of spirochætes or their toxins, from the whole superficies of the body and most of the internal organs. Thus, the posterior columns, which are in direct lymphatic connexion with the posterior roots, may be sensitized by the toxins of spirochætes ascending the afferent peripheral nerves; our explanation of the regional sensitization in tabes dorsalis corresponds to that given by Orr and Rows for the changes they have described in the posterior columns as a consequence of bed sores.

To explain the manifestations of dementia paralytica we again follow the views of Orr and Rows; sensitization of the essential tissues of the brain may arise from an affection of the lymph system of the cranial nerves by spirochætes or their products. It is possible, however, that in some cases sensitization may follow an infection of the intracranial tissues during the secondary period. A considerable amount of clinical and pathological evidence has now been collected to show that a meningitis is not uncommon in the acute stage of syphilis. Should this infection lead to the spread of spirochætes amongst the essential tissues of the brain, it would doubtless leave them, equally with the meninges, in a hypersensitive condition.

If now a spirochæte which has remained dormant, or has been active in some indifferent part of the body, appears among these sensitized nervous tissues, two different phenomena may be observed according to the site of its activity. If within the lymphatic area of the posterior columns, a violent reaction may ensue, injuring the nerve-fibres and producing proliferation of the neuroglia and wandering cells. The injury to the nerve-fibres will lead to degeneration, and this will continue as far as the reflection of the neurilemma and no further. When this stage has been reached, the process is at an end so far as concerns this particular region; in this sense tabes dorsalis is not a progressive degenerative lesion.

If the renewed activity of the spirochæte, however, happens to occur in the cerebrum, a similar reaction will take place in the nervous and other tissues, but, owing to the greater diffuseness of the sensitization, the area affected will tend to be greater. All intrinsic fibres within the sphere of reaction will tend to degenerate, but the process can seldom be observed to the end, owing to the involvement of vital functions and the early death of the patient.

The "parasyphilitic" reaction need not, however, be confined to these two areas. Isolated collections of cells, for instance those of the

anterior horn, may be affected and give rise to "parasyphilitic" muscular atrophy. Other groups of fibres or cells, alone or in combination, may be involved in the reaction according to the site of reappearance of the spirochæte, and so determine the clinical manifestations in each case of parasyphilis.

It will be recognized that antisyphilitic treatment can have no direct effect upon such degenerating nerve-structures, and therefore upon the symptoms and signs of tabes dorsalis or dementia paralytica; nevertheless, it may prevent the occurrence of a further reaction in another area by killing the spirochætes.

The fact, however, that antisyphilitic treatment has little or no effect upon the Wassermann reaction in dementia paralytica and in tabes dorsalis, must be explained on other grounds. It is possible that the degeneration of the nerve tissues continues the type of the initial reaction, and is thus "specific," giving rise continually to the Wassermann body. On the other hand, a more probable explanation is to be found in the fact that antisyphilitic remedies do not readily obtain access to spirochætes lying in the nerve-tissues; indeed, W. H. Willcox [quoted in 15] has already demonstrated that, after treatment with salvarsan, though all the viscera contained large quantities of arsenic, it was entirely absent from the brain.

If, then, the focus of origin of the Wassermann substance lies within the essential tissues of the central nervous system, it will not be exposed to the action of antisyphilitic remedies, and will remain active in spite of treatment. Thus, the cellular infiltration of the meninges, dependent on the activity of this focus, will also remain unaffected by treatment and will determine that injury of the pial covering which allows the passage of the Wassermann substance into the cerebrospinal fluid.

"Parasyphilis," as we have endeavoured to show, depends upon an anaphylactic reaction in the tissues of the central nervous system, which have been rendered hypersensitive in accordance with their peculiar lymphatic distribution. "Parasyphilis," therefore, does not differ from "chronic cerebral syphilis" in any essential pathological particular. It is merely a similar reaction in a different tissue. The word "parasyphilis" suggests a concept which is entirely foreign to our view of the nature of these morbid processes; it should therefore be confined solely to the multifarious clinical manifestations which may arise from the reaction of hypersensitive nerve-tissues and neuroglia to the *Spirochæta pallida*.

Conclusions.

(1) Parasyphilis of the nervous system is a purely clinical conception. It is a diseased state which may affect any part of the brain or spinal cord; the manifestations of tabes dorsalis and dementia paralytica can only be erected into two clinical divisions by an arbitrary selection of signs and symptoms. Some forms of progressive muscular atrophy, lateral and combined sclerosis, primary optic atrophy and periodic epileptiform attacks may be equally definite manifestations of parasyphilis.

(2) Parasyphilis is slightly, if at all, amenable to antisyphilitic treatment with compounds of arsenic and mercury, probably because these bodies do not enter the essential structures of the central nervous system.

(3) Parasyphilitic states are peculiarly liable to arise after mild syphilitic infection. Sixty per cent. of cases of tabes dorsalis have suffered from at most a primary sore, and in many instances the whole course of the initial infection was run under cover of a gonorrhœa.

(4) In dementia paralytica and in active, untreated cases of tabes dorsalis and tabo-paresis, the cerebrospinal fluid yields a positive Wassermann reaction, often of great strength.

(5) With acute or chronic syphilis of the nervous system, other than parasyphilis, the behaviour of the cerebrospinal fluid depends upon the extent to which the spinal cord and its membranes, including those of the brain-stem, are affected. Thus, most cases of meningomyelitis show a strong positive reaction in the cerebrospinal fluid, whilst cerebral lesions tend to give a weakly positive or even a negative reaction.

(6) Antisyphilitic treatment has a profound effect on the positive reaction in syphilitic meningomyelitis, and the cerebrospinal fluid may give a negative reaction after a few months.

But in cases of parasyphilis no obvious change occurs in consequence of such treatment, within any comparable period.

(7) Whatever views may be held of the primary and secondary manifestations in syphilis, we believe that all tertiary and "parasyphilitic" manifestations are expressions of the reaction of hypersensitized tissues ("hyperallergie"). That is to say, during the previous stages of infection, the tissues have been so altered that they react more violently to a smaller dose of the spirochæte or its toxins.

Gummatosis is the reaction of hypersensitized connective tissues and blood-vessels, whilst "parasyphilis" is a hyperallergic reaction of the essential nerve-elements and neuroglia.

(8) The consequences of this hyperallergic reaction in the tissues of the central nervous system is death of any set of fibres or cells which happens to be attacked, and proliferative reaction on the part of the neuroglia within the same territory.

Thus, the clinical manifestations of "parasyphilis" are an expression of the reaction and necrosis of hypersensitized areas of the nervous system, evoked by reappearance of the *Spirochæta pallida*.

(9) This hypersensitive ("hyperallergic") state of the tissues of the central nervous system is produced, in all probability, by the passage of the spirochætes or their toxins up the nerves from the skin and mucous membranes during the secondary period. But it is also conceivable that it may be due to a slight "encephalitis" during this stage of infection.

The headache and lassitude, unaccompanied by any gross nervous lesions, which so frequently occur during the secondary stage, possibly represent clinically the period during which sensitization occurs.

(10) Thus, parasyphilis is a clinical conception which comprises the manifestations of a series of diseased states. From the pathological point of view, the term is inadmissible. These states depend on the reaction of hypersensitized tissues to the spirochæte or its toxins, and this reaction is as truly syphilitic as the production of gummata.

The difference between the consequences of the tertiary and of the "parasyphilitic" process lies in the nature of the tissues participating in the reaction. In the one case the connective tissue is capable of repair, and the focus is readily reached by the remedial agents. In the case of "parasyphilis," reaction of the essential nerve-elements leads to their death, and antisyphilitic remedies cannot readily reach the spirochæte.

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THE BRAIN OF A MACROCEPHALIC EPILEPTIC.

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AND

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PART I.—CLINICAL HISTORY.

THE subject of this communication was a male epileptic who was admitted into Rainhill Asylum under our care in August, 1901, and died there in January, 1910. He was a single man, by occupation a piano-tuner, and his age on admission was 28. His family history was good. His father was an intelligent man, a Non-conformist minister, and there was no record of insanity, epilepsy, or allied neuroses in the family. The patient himself had always enjoyed

good health, and had never had any serious illness except an attack of pleurisy. He was bright and intelligent as a child, and early showed promise of great musical ability, but he was always of a nervous, excitable disposition. At the age of 9 years he seems to have had an attack of *petit mal*, but the first distinct fit occurred when he was 16, and since that time he remained subject to epileptic attacks at variable intervals. For about a year before admission, the parents of the patient had noticed a gradual mental deterioration, which doubtless had been coming on insensibly for some time previously, but no attack of active insanity occurred until ten days before admission, when he became delusional, excited and threatening, which necessitated his removal to the asylum. He was on admission a man of good physique, 5 ft. 10 in. in height, and 12 st. 10 lb. in weight, with all his viscera apparently healthy. The limbs were well formed and symmetrical; there were no deformities of any kind. The circumference of his head was 25 inches. His mental condition was one of partial dementia. He was dull and weak-minded generally, slow of speech with prolonged reaction time, but was nevertheless fairly intelligent, could give a good account of himself, and was a useful worker. His history thenceforward was that of epileptics generally. The frequency of his fits increased in spite of treatment by bromides, so that whereas in the year 1902 his fits had averaged 5·9 per month, these had increased in 1907 to 9 per month. Along with this went steadily increasing impairment of memory and intelligence; he also had periodical attacks of excitement, lasting for a few days at a time, during which he was violent and dangerous, such attacks usually leaving him on their subsidence somewhat duller than before. Even when at his best he was markedly irritable and quarrelsome and showed much emotional instability. The steady mental deterioration was well shown by the fact that when first admitted into the institution in 1901 he was a useful worker in the place, but by the end of 1906 he had become useless as such, and in 1909 he had not sufficient mind to employ himself in any way. Concurrently with this his health gradually failed, and he finally died of an attack of broncho-pneumonia at the age of 37.

Autopsy Notes.

Autopsy twenty-two hours after death. Temperature of mortuary 40° F. Height 69½ in.; circumference of shoulders 35½ in.; of head 25½ in. No deformities. Skull markedly dolico-cephalic and

symmetrical; density average; average frontal thickness 6 mm.: occipital 8 mm. Dura mater congested, of normal thickness. The superior longitudinal and lateral sinuses contained dark fluid blood. Sub-dural fluid clear and in slight excess. Pia-arachnoid very congested and somewhat œdematous but showed no abnormal opacity; it stripped from the hemispheres a little more readily than naturally in the frontal region and about naturally elsewhere.

The brain generally was rather soft in consistence and somewhat œdematous. There was slight general wasting of the prefrontal region of both cerebral hemispheres but little or no obvious wasting elsewhere, and there were no local surface softenings. The lateral ventricles were slightly dilated, with slight excess of clear fluid. Large granulations were present in the third ventricle, anterior part of the lateral ventricles and in the lateral angles of the fourth ventricle. The main cerebral arteries were normal in distribution and appearance; veins congested.

The bodily organs generally were congested but showed no features of interest. The internal secretory organs all appeared to be normal. Areas of broncho-pneumonia were present in both lower lobes and a few patches of early atheroma in the thoracic and abdominal aorta, mostly in the latter. There were no signs of syphilis.

Weights of organs in grammes: Right lung 730; left lung 700; heart 235; liver 1,100; spleen 125; right kidney 155; left kidney 155.

The weight of the encephalon, immediately after removal from the body:—

Total weight, unstripped of membranes			2,130 grm.
Right hemisphere unstripped ...	947 grm.;	stripped	918 grm.
Left „ „ ...	924 grm.;	„	900 grm.
Cerebellum, pons and medulla, unstripped			228 grm.

The encephalon in this instance is thus 730 grm. above the average weight of the unstripped male encephalon, viz., 1,400 grm., as given by Marchand [14]. It may be calculated from Marchand's figures that 609 grm. is the average normal weight of each unstripped cerebral hemisphere. In this specimen this weight is exceeded by 338 and 315 grm. in the right and left hemispheres respectively.

The difference in weight of 23 grm. between the right and left hemispheres can scarcely be looked upon as unusual in view of the large size of the hemispheres, nor can the loss of 29 and 24 grm. occasioned by stripping the right and left hemispheres respectively, as 20 grm. is approximately the amount which the normal hemispheres lose in weight on stripping.

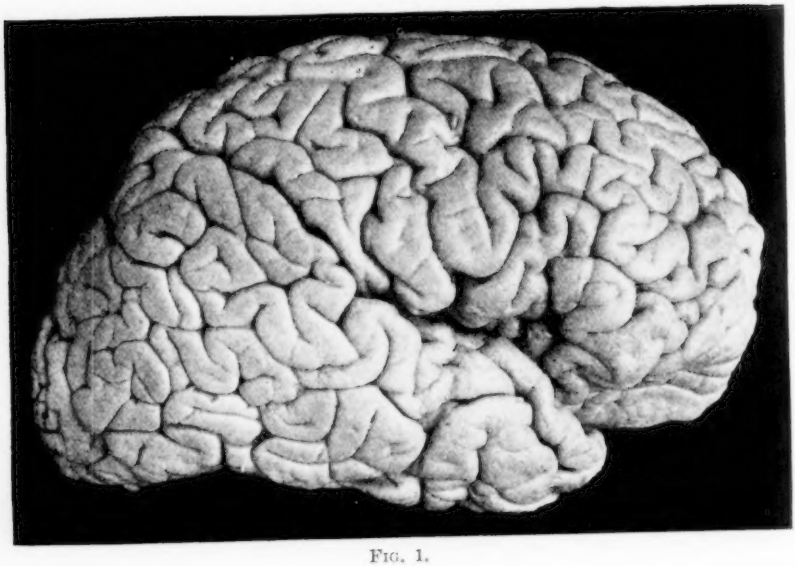

FIG. 1.

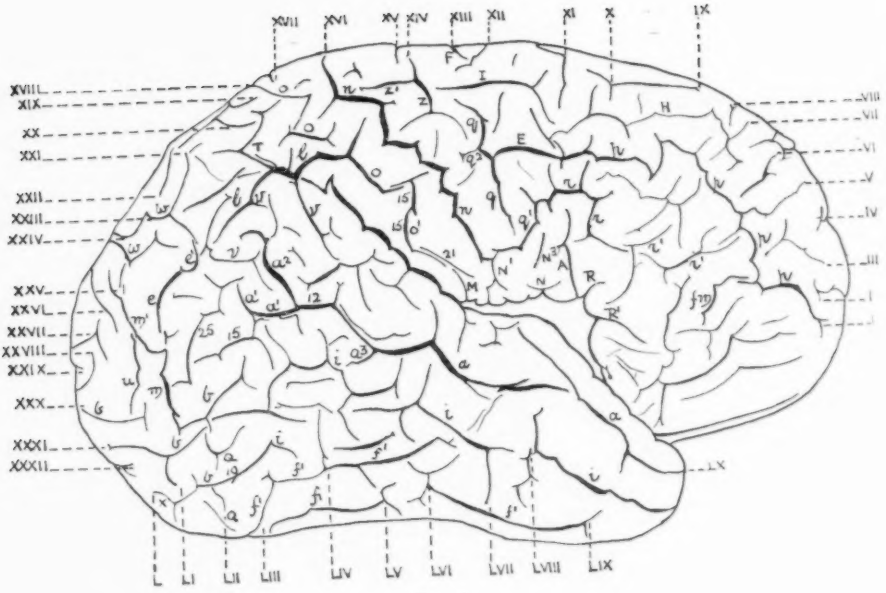
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FIG. 1*a*.

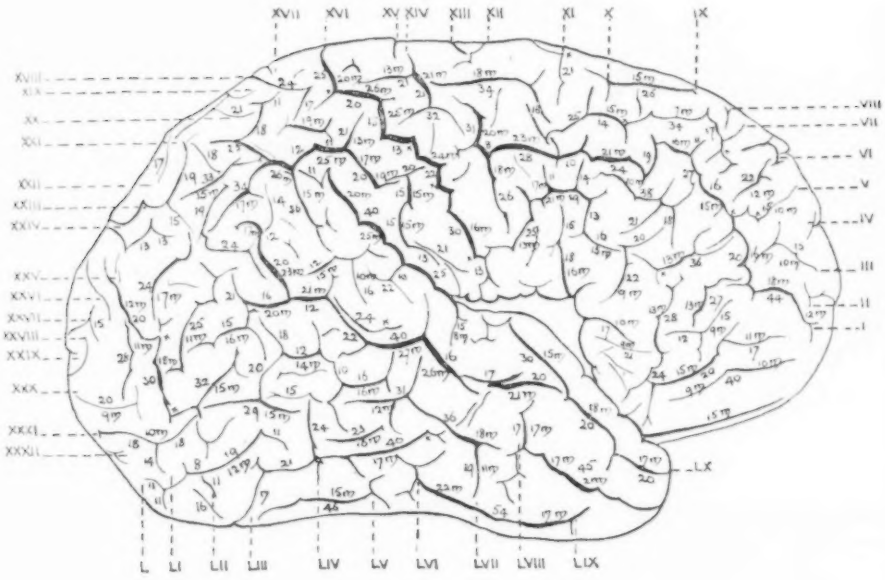
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FIG. 1*b*.

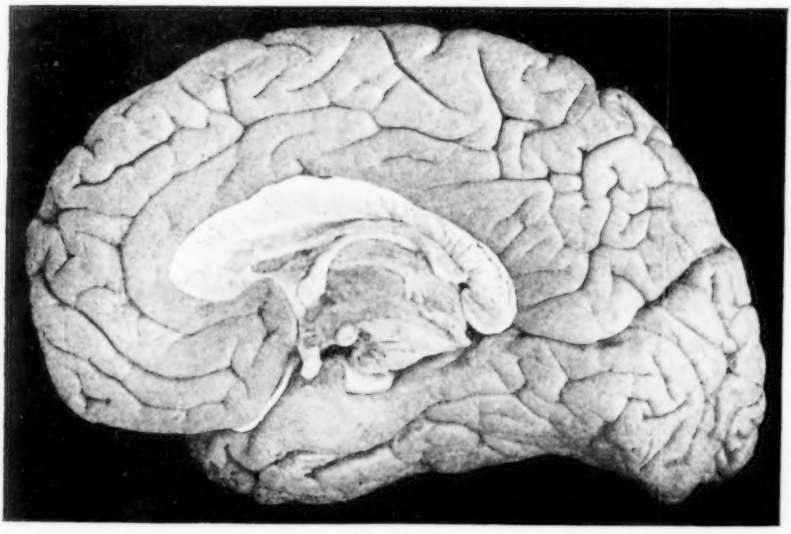

FIG. 2.

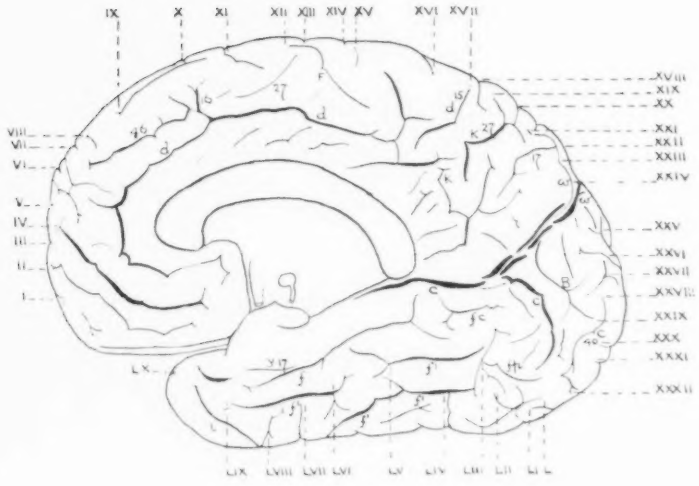

FIG. 2a.

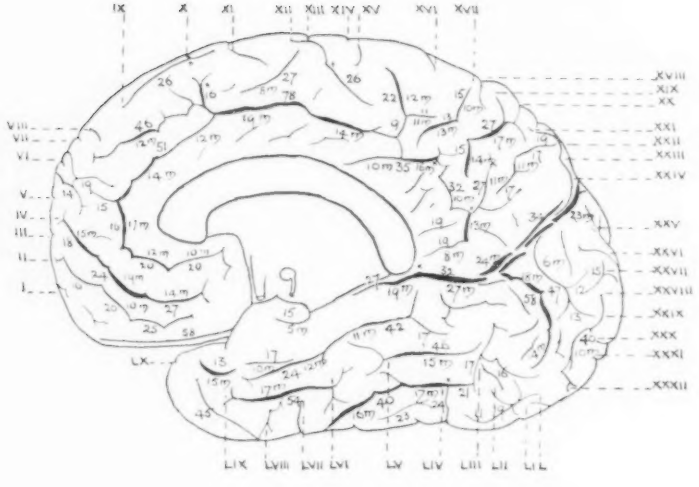

FIG. 2b.

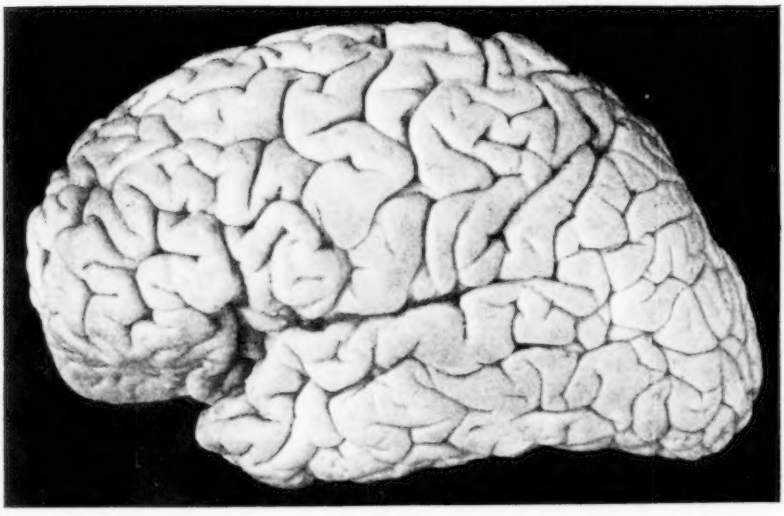

FIG. 3.

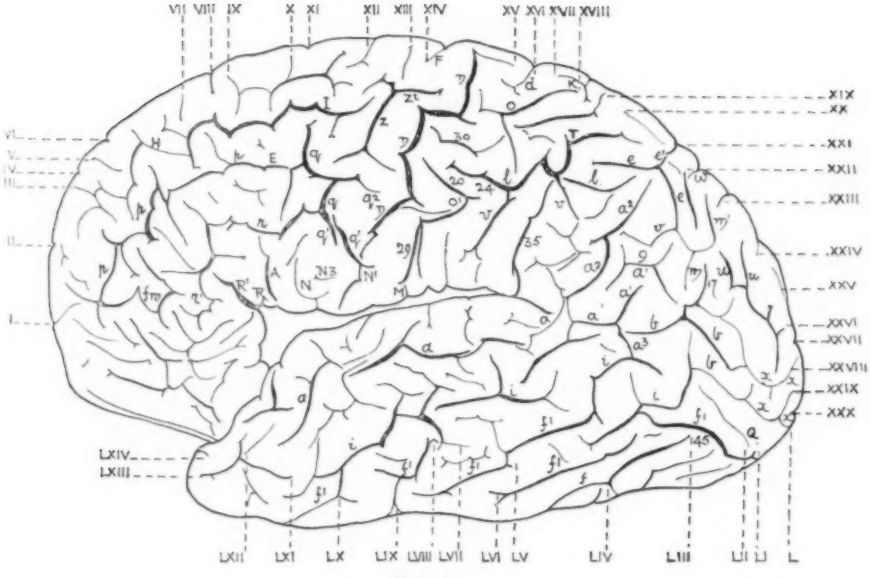
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FIG. 3a.

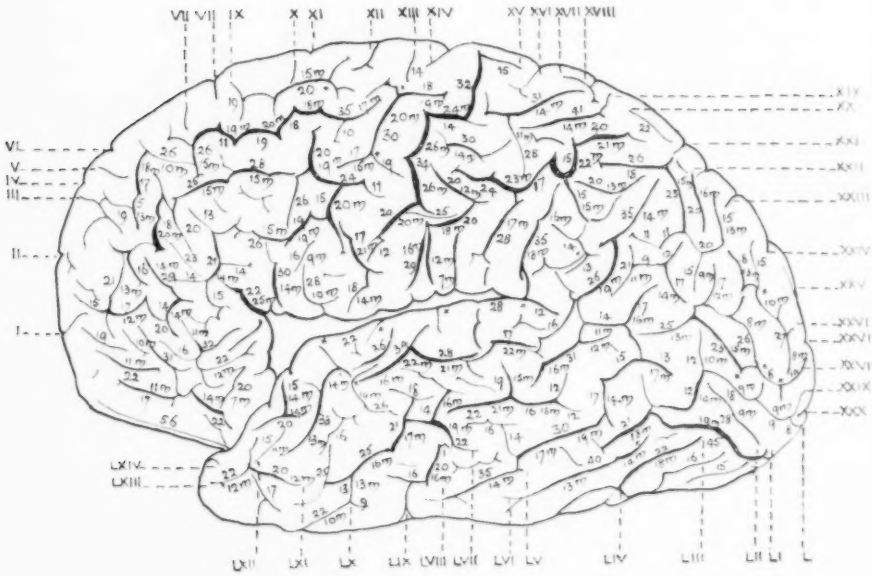
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FIG. 3b.

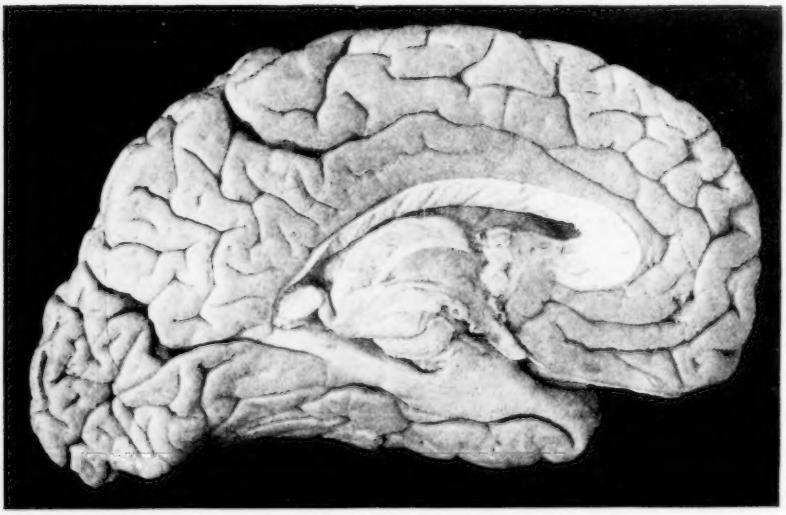

FIG. 4.

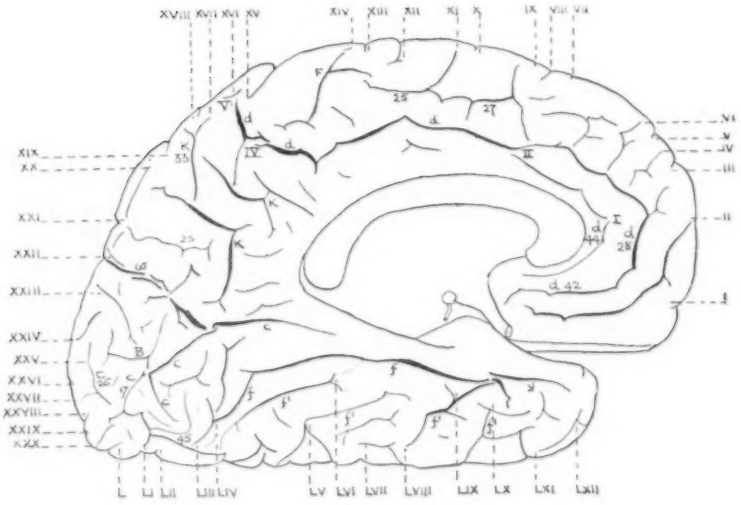

FIG. 4a.

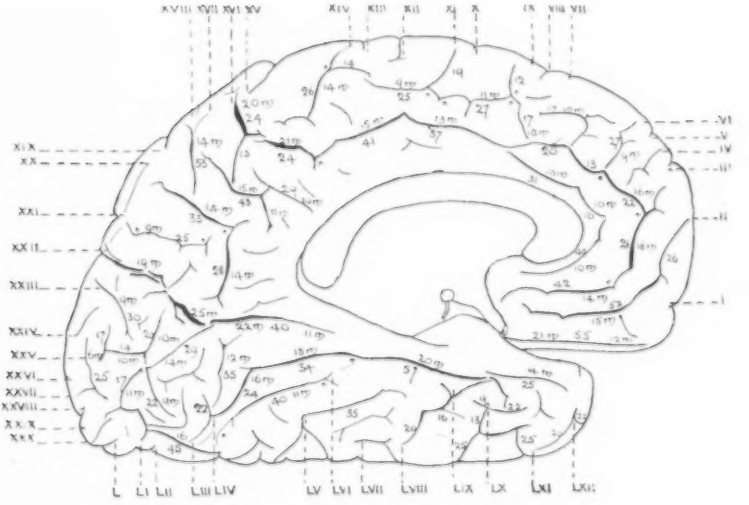

FIG. 4b.

The normal ratio of the conjoined cerebellum, pons, and medulla to the cerebrum is given by Huschka as 13 : 87. In this specimen, the ratio being 10·6 : 87, the weight of the cerebrum relatively to that of the conjoined cerebellum, pons, and medulla is in excess of the normal.

FIG. 5.

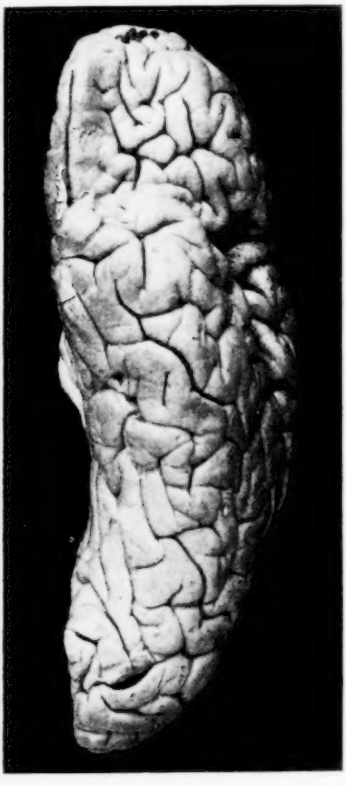

FIG. 6.

Looked at *generally* the cerebral hemispheres are unusually long as compared with their breadth. The different parts, however, appear to be in about normal proportion, excepting that the fronto-polar region on each side strikes one as being decidedly broad, relatively as well as absolutely, the superior portion of each third frontal gyrus is somewhat defective, and occipital lobes are relatively somewhat small.

The cerebellum, pons, and medulla appear as regards their shape and constitution to be in every way normally developed, and these parts are well covered by the cerebrum.

The encephalon is one of the largest—uncomplicated by any gross pathological change—of which there is any authentic record.[1] It is of interest to note that in several instances which have been reported of extraordinarily heavy brains the possessors have suffered from epilepsy.

The encephalon in this case much exceeds in weight that of the great majority of the 108 eminent men whose brain weights have been collected by E. A. Spitka [18], the nearest approach to it, in regard to weight, viz., 2,012 grm., being that of Turgenev, the Russian poet and novelist. The cerebral hemispheres are also, on the whole, about the most generally complex in pattern which we have hitherto seen. So far as can be judged from the drawings they are more complex than are those of any of the eminent men illustrated in Spitka's work, either those specially described by himself or by Retzius and others.

The Drawings of the Cerebral Hemispheres.

As illustrations supplementary to the photographs, drawings have been prepared something after the manner of Kohlbrugge [12] and [13] and of Cole [8]. These are freehand drawings based upon tracings of the photographs of the hemisphere. In the case of the lateral surface a considerable extension has been made towards the boundaries of the tracing so as to obtain in a single picture complete, or almost complete, views of the orbital surface, and of the fronto-polar and occipito-polar regions, as well as of the dorsal aspect of the hemisphere. The mesial aspect is shown in a similar manner, but as so much more of this surface, as compared with the outer, is almost flat a much less extension towards the boundaries of the drawing has been necessary. The drawings are thus, as Cole states with reference to his own, "a sort of Mercator's projection, though, of course, not mathematically exact. . . . The

[1] We have been able to find records of three human brains only, whether accompanied by pathological changes or not, of greater weight than the one under consideration, although it is possible that there are others which have escaped our search. These three are as follows:—

(1) Van Walsem's [22] case—2,850 grm.

(2) Sims' [17] case—2,400 grm. (Quoted by Anton [1] and Kohlbrugge [12].)

(3) A case mentioned by Hermann Pfister [16] 2,222 grm. There are reasons, however, for believing that there were gross pathological changes in this case.

longitudinal dimensions of the parts about the crest of the hemisphere are unavoidably exaggerated . . . but their transverse dimensions, radial in the drawing, are given as nearly as possible in their true proportion."

The drawings differ from those of Kohlbrugge and Cole in that an attempt has been made to give an adequate display of the sulci and gyri of the under surface of each hemisphere by making a considerable extension in this direction of the drawings of the lateral and mesial aspects. The position of borders, such as the superciliary and occipito-temporal, can be seen on comparison with the photographs.

The drawings are in three sets. In one set (figs. 1*b*, 2*b*, 3*b*, 4*b*), the Arabic numerals *without* the letter *m* adjacent to them show the estimated length in millimetres of the different sulci, or portions of these, against which they are placed. A small + is put against a point from which a portion of a sulcus was measured to its extremity or from point to point along the sulcus. These measurements thus do not convey the idea of length from point to point, but from them may be gathered the estimated length of a sulcus. The extent to which the drawings are necessarily inexact in certain places can be seen from these measurements.

The drawings give a more accurate idea of the composition of the sulci than do the photographs; annectants are usually more clearly indicated, and the representation of mere vascular grooves, which may appear as shallow sulci in the photographs, is omitted from the drawings.

The Arabic numerals *with* the letter *m* adjacent to them indicate the estimated depth, in millimetres, of the several sulci at about the points against which the numerals are placed. Owing to obvious difficulties, however, all these measurements can only be regarded as approximately correct, and are merely of relative value.

The Roman numerals have been employed after the manner of Kohlbrugge and of Cole (the former uses Arabic numerals for this purpose) as marks by which one may identify corresponding points in two views of the same hemisphere. For facility of reference in these very complex hemispheres a considerable number of these points have been indicated. Many of the sulci, or portions of these, appearing in different views of the same hemisphere may also be identified by the Arabic numerals placed against them.

In another set of drawings, viz., figs. 1*a*, 2*a*, 3*a*, 4*a*, the sulci, the identification of which is certain, or fairly certain, have letters placed

against them corresponding to the letters used by Kohlbrugge in his drawings. For the sake of clearness all the numerals referring to measurements have been omitted in this set of drawings excepting certain Arabic numerals, similar to those employed in the first set of drawings, which have been placed against certain sulci referred to in the text, the identification of which is doubtful, or to which special attention is directed.

The third set of drawings, figs. 7 and 8, will be referred to under Part II.

Method of Hardening the Cerebral Hemispheres.

The cerebral hemispheres were hardened in 5 per cent. formalin after being stripped of their membranes, each hemisphere being laid on its mesial surface supported by wool. This method was adopted because it was originally intended to attempt micrometric measurement of sections from various regions of the cortex, and in order to obtain results comparative with other control cases it was considered advisable to strip the cerebrum in the fresh state. Unfortunately, although the tissue was fairly satisfactory for ordinary microscopical examination, it was found to be unsuitable for micrometric measurement.

Measurements of the Cerebral Hemispheres.

These are in three sets. The second and third sets, particularly, have been made according to E. A. Spitka's [18] system. This author states that those measurements are best which can be reduced from absolute to relative values wherein some unit of length, preferably the maximum cerebral length, is used as a basis of expression rather than so many inches or centimetres. Hence centesimals of the length of the cerebrum are used, so that all brains may be compared, "no matter what their size or what the degree of shrinkage may be, so long as there is no actual distortion."

The method of hardening above described unavoidably leads to a certain amount of distortion of the hemispheres. Consequently it is doubtful if the measurements of these given below are of much value, partly for this reason and partly because of the difficulty of finding fixed points. In fact some writers advocate the abandonment altogether of any attempt at such measurements, believing that they are not only worthless but actually misleading. It is possible, however, that such measurements would be of some interest and value if compared with corresponding ones made upon hemispheres hardened in a similar manner, and which were originally not markedly atrophied or soft and flabby.

Measurements of the Cerebral Hemispheres.

Compared with the average measurements, when obtainable, of the brains of ten ordinary and normal individuals (Spitka [18]). All the measurements are given in millimetres.

	Right hemisphere	Left hemisphere	Average when obtainable
I.—Principal diameters, &c.			
Maximum length	216	223	172
Maximum width	65	59	—
Maximum width of cerebrum 124	—	—	139
Cerebral index $\left(\frac{\text{Breadth} \times 100}{\text{Length}}\right)$ .. 55·6	—	—	81
Maximum depth	140	136	—
Mesial length	382	380	—
Lateral length	270	275	—
Callosal length	103	113	—
Precallosal length	42	38	—
Postcallosal length	81	82	—
Occipito-temporal length	172	173	—
Sylvian angle	45°	28°	—
Rolandic angle	66°	64°	—

			R.	L.
II.—Arc measurements, along the dorsi-mesial border.				
Frontal arc	235	237	155	155
Parietal arc	79	79	55	57
Occipital arc	80	85	59	57
Cerebral indices (expressed in centesimals of the total fronto-occipital marginal arc)—				
Frontal index	59·6	59·1	57·7	57·7
Parietal index	20·1	19·7	20·4	21
Occipital index	20·1	21·2	22·1	21·3

III.—Horizontal distances (expressed in centesimals of the hemicerebral length).				
From cephalic point to—				
Lateral aspect: (1) Tip of temporal lobe	20·3	22·4	23	24
Lateral aspect: (2) Sylvian-presylvian junction	28·7	32·2	30	30·4
Lateral aspect: (3) Ventral end of central fissure	40·7	40·8	42·2	44·4
Lateral aspect: (4) Sylvian-episylvian junction	55·1	51·5	55·9	60·5
Lateral aspect: (5) Caudal point	—	—	100	
Mesial aspect: (6) Frontal edge of callosum	19	16·5	—	22
Mesial aspect: (7) Porta (foramen of Monro)	34·2	36	—	41·2
Mesial aspect: (8) Dorsal end of central fissure	69	67·6	—	63·9
Mesial aspect: (9) Dorsal intersection of paracentral fissure	74	70·2	—	68·2
Mesial aspect: (10) Caudal edge of callosum	65·7	66·2	—	64·2
Mesial aspect: (11) Occipito-calcarine junction	79·6	79·5	—	74·7
Mesial aspect: (12) Dorsal intersection of occipital fissure	92·5	90·3	—	86·2

Whatever view may be taken of the value of these measurements, a brief allusion may be made to one or two points revealed by them.

The length of the hemispheres as compared with their breadth is very great, so that the cerebral index, viz., 55·6, is remarkably low. This cannot be wholly accounted for by the method of hardening adopted, i.e., by a tendency for the hemisphere to spread out flat and thin when lying on its mesial surface. It is almost certain that the latter method has some influence in reducing the cerebral index, particularly in the case of brains which show much wasting and dilatation of the lateral ventricles. Yet the cerebral index in this specimen, which was little wasted, is decidedly smaller than is that of any of the other brains in our possession which were hardened in a similar manner, and which were measured for comparison, in spite of the fact that many of these control brains were much atrophied.

The measurements (6, series III) would suggest that the mesial part of the frontal lobe in front of the corpus callosum is relatively rather small, especially in the left hemisphere, but the remainder of the frontal lobe is in almost normal proportion.

The occipital index apparently shows that the occipital lobe is relatively rather small, especially on the left side.

Other departures from the average in the measurements may perhaps be accounted for, or at least partly so, by a certain amount of distortion of the hemispheres.

General Account of the Cerebral Hemispheres.

In view of the clearness and sufficient accuracy with which the course and dimensions of the sulci are represented in the drawings, no systematic description of these or of the gyri appears to be necessary. The following general account will serve to direct attention to the main features shown by the convolutional pattern of the hemispheres. The identification of the sulci has been in some instances a matter of considerable difficulty, and we are much indebted to Dr. S. J. Cole for valuable help in this connection. Dr. Kohlbrugge has also kindly revised the lettering of the sulci. We are ourselves, however, entirely responsible for all the opinions expressed.

In addition to comparison with the descriptions and drawings of the sulcal pattern of the numerous cerebral hemispheres given by Kohlbrugge [12] and [13], indications of departure from the usual and normal brain pattern, such as are regarded of importance by many other observers, have been carefully looked for. These have been summarized by Mickle [15] as occurring in the following directions: (1) In superiority, indicating active development and high evolutionary grade. (2) In

aberrant irregularity and bizarre arrangement of the sulci and gyri, which is taken to signify formative activity, or over-activity but ill-directed. (3) In inferiority by defect: (*a*) either as a developmental defect, so that there is persistence, more or less, of fœtal characters in place of advance to adult form: (*b*) or as an evolutionary reversion to brain types of lower races of mankind, or to lower animal types.

The Sulci and Gyri of the Cerebral Hemispheres.

We will deal with the interlobar fissures first, and then with the sulci and gyri of the several lobes.

The Interlobar Fissures.

The fissure of Sylvius.—The general course of this fissure is more steeply inclined on the right side than on the left, but this is usually regarded as a normal difference between the two hemispheres both in man and in most of the apes; the macaque, according to Cunningham [9], showing an exception in this respect.

The main portion of the posterior limb of the fissure is, as is usual, considerably longer on the left side than on the right. The posterior limb ends on both sides in a shorter descending and a longer ascending ramus. It seems doubtful how much of the latter really belongs to the Sylvian system. It is broken by several deep interdigitations, and just above the mark 35 in the left hemisphere, and at a corresponding place in the right is a deep gyrus. Probably only the lower piece of the apparent ramus, below the deep gyrus, belongs to the Sylvian; the upper piece being a subsidiary sulcus of the inferior parietal lobule, although it does not actually join the sulcus interparietalis.

In the right hemisphere the anterior limb possesses two rami, a posterior one, R, which is short and deep—the apparent sulcus seen in the photograph joining this is merely a vascular groove—and an anterior one, R^1, having a forward and downward direction. On the left side the anterior limb shows only one well-formed ramus, R^1, the sulcus behind this, R, representing the ascending ramus, being quite small. Further reference to these rami is made on p. 51.

The sulcus centralis, n. N^1.—This sulcus follows a fairly usual course on both sides, excepting that in the right hemisphere it is straighter than is common, and the typical backward extension of its upper extremity is absent. Each sulcus shows several deep annectants,

and the upper and lower buttresses of Symington and Crymble [19] are rather more distinct on the right side than on the left.

The small sulcus, lettered N^1, when in the position it occupies in these hemispheres, should probably be regarded as part of the s. centralis, for we have found in several cases that a similar sulcus forms a posterior limit to the Betz-cell area. The sulcus in question is on the left side, separated from the *n* sulcus by a narrow superficial bridge—the lower bridge of Mickle [15]. The presence of such a bridge, if broad, would probably be a mark of inferiority.

Superficial union of the right s. centralis with the s. precentralis, and with the Sylvian, by means of an intermediary sulcus (N^1) may also be noticed. This union, when present, is regarded by Mickle as aberrant.

A short, straight, smooth-walled s. centralis shallow relatively to the s. interparietalis resembles that of lower apes, and it has been asserted that in poorly-developed brains and in those of negroes the s. centralis is less sinuous than normal. But Mickle [15] states that this condition is not often a criterion of low type, for some decidedly inferior brains have sinuous or zigzag central fissures. In this case the right s. centralis, although rather straighter than usual, is of relatively good length, is of good depth, and possesses well-marked deep annectants.

The fossa parieto-occipitalis, w.—This is well closed on both sides. The sulci composing the complex, as seen on opening up the fossa, are somewhat diagrammatically shown in the drawings, for all the internal annectants are deeply placed. On the right side the dorsal elements forming the incisura are two in number (*w*, *w*) and the anterior of these especially is of considerable length. On the left side there is only one dorsal element, and this is short. The cuneo-limbic and cuneo-precuneal annectants are deep, and are very similarly disposed on the two sides.

The sulcus calcarinus, c. Right hemisphere.—The anterior portion or stem passes forwards for a somewhat unusual distance anterior to the splenium of the corpus callosum. The posterior portion curves markedly downwards and backwards in the main part of its course, its lower end bending slightly forwards. It is separated posteriorly by a broad superficial posterior cuneo-lingual annectant from an undulating sulcus (marked *c* 40), which also probably forms part of the calcarine system. The anterior cuneo-lingual annectant is somewhat small, and is for the most part deeply placed. Three small deep interdigitations are seen along the course of the posterior calcarine proper.

Left hemisphere.—The stem of the sulcus follows a usual course. The posterior division passes at first downwards and backwards, and then makes a sudden bend downwards and slightly forwards—the general direction of this portion of the sulcus being very similar to that on the right side. The small sulci behind (marked *c* 17 and *c* 25) probably also belong to the calcarine system. The anterior cuneo-lingual annectant is small and deeply placed, the posterior is superficial and narrow.

In both hemispheres the stem of the sulcus shows the normal obliquely downward cut into the brain substance, whilst the posterior portion, as is usual, incises the cerebrum at about right angles to the surface.

On the right side the posterior calcarine proper ends rather further forwards than is common in the well-developed human brain. This, together with the presence of the curving shallow sulcus behind, separated by a broad superficial annectant, may possibly be some indication of a phylogenetic reversion.

In the left hemisphere the irregular arrangement of the posterior calcarine and of the separate terminal pieces behind this is atypical, and perhaps may be regarded as a sign of aberrancy and inferiority.

The sulcus collateralis, f, fc; and *sulcus rhinalis, y.*—The right s. collateralis must probably be regarded as being defectively developed. It is in two pieces separated by a broad superficial annectant. Both portions of the sulcus are unusually shallow and are smooth walled. The sulcus marked *y* 17 represents a s. rhinalis; between this and the main portion of sulcus *f* is a narrow superficial gyrus rhinencephalo-temporalis posterior. There is in this hemisphere a short incisura temporalis.

The left s. collateralis is better developed than is the corresponding sulcus of the right side. It has a fairly usual course: is of good depth and shows three deep interdigitations in its posterior portion. The sulcus marked *y* represents a s. rhinalis and there is a fairly broad gyrus rhinencephalo-temporalis posterior, for the most part deeply placed, and a narrow gyrus rhinencephalo-fusiformis. No distinct incisura temporalis is seen in this hemisphere. The sulcus rhinalis on both sides probably forms a partial boundary to Brodmann's area of cortex No. 28.

The sulcus cinguli, d. Right hemisphere.—The pars anterior and pars intermedia are typically placed. No definite Brücke of Eberstaller is seen along the course of these portions of the sulcus, although several

small deep interdigitations are present. The pars posterior (*d* 15) is separated from the pars intermedia by a broad superficial annectant representing either Brücke III or IV whilst a Brücke V (the gyrus arcuatus anterior of Retzius), arches round the upper end of the pars posterior. The pars intermedia forms a definite junction with the sulcus subparietalis (K) (see fig. 2*b*). Such a union is shown in some of the drawings by Kohlbrugge [12] and [13] of Malayan and Javan brains. It is looked upon by Mickle [15] as aberrant in the human brain and as pointing to a phylogenetic reversion, although probably a junction of the *K* sulcus with the pars posterior of the sulcus cinguli would be of greater significance in this respect.

Left hemisphere.—The anterior reaches of the sulcus in this hemisphere must probably be looked upon as being duplicated, the sulcus marked *d* 28, 42 forming a s. cinguli superior. But below and behind this, and having a somewhat similar direction in relation to the genu of the corpus callosum, is another but much shallower sulcus (*d* 44) which may be regarded as part of the sulcus cinguli. There are several deep interdigitations, but no definite Brücke occurs along the course of the pars intermedia and sulcus *d* 28, 42. But the lower and posterior sulcus, *d* 44, has an almost superficial annectant crossing it at the mark I, and it is separated from the pars intermedia by a surface annectant at the mark II. If this sulcus, *d* 44, be regarded as part of the s. cinguli then these annectants have the usual position of Eberstaller's Brücke I and Brücke II respectively. The pars posterior is in two divisions—horizontal and ascending—separated from each other by a Brücke IV. A Brücke V is also present.

Duplication of the forepart of the s. cinguli appears to be commoner in the left hemisphere than in the right (Mickle [15] and Kohlbrugge [12] and [13]), and, when present, may be regarded as a normal difference between the two hemispheres.

Mickle [15] states that it is not infrequently difficult to appraise correctly the significance of certain appearances of the sulci. "Like words in a sentence, their meaning varies with the context." Duplication or triplication of the sulcus cinguli may be taken as a case in point. This may sometimes mean the abnormal persistence in the adult of a fœtal character, and at other times aberrant formative activity, but such interpretations can probably only be placed upon the appearance if accompanying conditions show a defective, reverting or aberrant tendency. If these conditions evince a normal or high brain type, the duplication of the sulcus in question may probably be deemed to manifest fissure wealth.

The Frontal Lobes.

The external Surface.—The *precentral* system of sulci (F, *z*, *zi*—*q*, q^2,q^1) is well developed and is for the most part typical on both sides. The sulcus F, placed rather far forward in the right hemisphere, is a good example of the solco inflesso of Lussana, or inflected fissure of E. A. Spitka [18] or s. præcentralis mesialis. The ramus sagittalis posterior (*zi*) of the s. præcentralis superior is well developed in both hemispheres.

The *s. frontalis superior* (I and H) is comparatively simple and shallow in the right hemisphere as compared with the left, probably in association with the especially good development of the mid-frontal system in the former hemisphere.

The *s. frontalis mesialis* is fairly well developed on both sides, rather better on the left than on the right.

The sulci *q* and q^2 represent the *s. præcentralis medius* of some authors. The ramus horizontalis anterior of Eberstaller forms an important branch of this sulcus.

The *p* system of sulci (in part the *s. frontalis medius*) is unusually well developed on both sides. In the right hemisphere the anterior portions of this system form a typical *s. fronto-marginalis*, consisting of a stem and a mesial branch. There is also a lateral branch (*fm*), separated from the stem by an annectant, but the mesial branch in this instance, as is commonly but not invariably the case, is obviously the direct continuation of the main stem. The stem and mesial branch well represent a sulcus identified by Bolk [3] with the *s. rectus* of lower apes.

On the left side the arrangement is not quite so typical. The stem divides into a shorter mesial and a longer lateral branch, and it is not clear which of these two is the direct continuation of the main stem.

The sulcus q^1—in part the *s. præcentralis inferior*—appears to be duplicated in the left hemisphere. The posterior of the two sulci superficially joins the N^1 sulcus, but a deep gyrus crosses the sulcus almost opposite the lower end of the *n* sulcus. On the right side the q^1 sulcus is single but is somewhat unusual. It appears to be a lower portion of the s. præcentralis inferior forming an aberrant though shallow connection with the *n* sulcus and with the Sylvian fossa by means of an intermediary sulcus N^1.

The *inferior frontal* system of sulci *r*, r^1 is fairly typical in both hemispheres, but on the right side the different elements of the system are separate from each other, whilst on the left side they are joined.

The *subfrontal* region—using the term subfrontal according to Brodmann's [6] meaning—is on the whole comparatively small and simply convoluted. The orbital (or inferior) operculum is well developed on both sides. On the right side the anterior limb of the fissure of Sylvius possesses two definite rami, R, R^1, enclosing between them a relatively moderate sized intermediate (or triangular) operculum. In the left hemisphere this operculum is decidedly small, as there is only one well formed anterior limb of the Sylvian complex. The latter arrangement is probably more common on the right side than on the left. The superior operculum is somewhat defective, especially in the right hemisphere. The amount of exposure of the insula as seen in the photographs and drawings is no doubt exaggerated owing to the membranes having been stripped from the hemispheres before hardening. This would probably affect the position of the temporal more than that of the frontal opercula, and owing to a certain defect of the intermediate and superior frontal opercula it is probable that in the natural state there was some undue exposure of the insula.

A *sulcus diagonalis* is not easy to identify with certainty in these hemispheres. As Kohlbrugge [12] and [13] has suggested (and Bolk [3] agrees), a true s. diagonalis is part of the s. præcentralis inferior which has become detached owing to the rising up of a gyrus in the depths of the latter sulcus. The sulcus lettered A in both hemispheres in this specimen may probably be regarded as a s. diagonalis owing to its position in front of the sulcus identified as the s. subcentralis anterior (N), and owing to the close proximity of its lower end to the anterior Sylvian ramus.

A remark may here be made concerning the *sulcus arcuatus*. Cole [8] believes that the upper or horizontal limb of the arcuate sulcus of lower apes is often represented in the human brain by a part of the s. frontalis superior. According to this view the course of the s. arcuatus would probably be represented in this specimen on the right side by the sulci lettered q^1, the lower part of q and H, and on the left side by those marked q, q and I.

The mesial surface. The marginal gyri and paracentral lobules.—This surface is comparatively simply convoluted in the right hemisphere. In the left fairly-well developed branches marked 25, 27, constituting the *mesio-frontal intragyral sulcus* of Mickle [15] or *fissure fronto-marginalis* of Spitka[1] [18], divide part of the marginal gyrus into

[1] *Sulcus gyri marginalis* would probably be a more appropriate name for this sulcus than fissura fronto-marginalis, in order to avoid confusion with the sulcus fronto-marginalis.

two tiers. This sulcus on the right side is represented by the shallow furrow marked 27, and possibly also by the furrow marked 46 which makes a shallow connection posteriorly with the branch of sulcus *d* marked 16. The sulcus appears often to be better developed in the left hemisphere than in the right in common with the more frequent duplication in the former hemisphere of the anterior reaches of the s. cinguli.

The sulcus L of Kohlbrugge (*cephalic paracentral* of Wilder, *s. paracentralis* vel *præparacentralis*) is not present in the left hemisphere, and the branch of sulcus *d* marked 16 in the right is probably placed too far forward to represent the sulcus. Kohlbrugge regards the sulcus L as of little importance.

The *rostral* sulci are long, simple and typically placed in the right hemisphere, but in the left, if the sulcus, *d* 28, 42 is to be looked upon as a s. cinguli superior, only one rostral sulcus is present.

The left paracentral lobule is smaller than the right and is smooth. On the right side the lobule is scored by a long branched upturn of the s. cinguli.

The orbital surface.—There is some tendency to keeling of this surface in both hemispheres. The orbital sulcus shows the usual transverse and sagittal elements. The transverse element is of great length on the right side, and its outer end passes over the superciliary border for a considerable distance. The whole system, however, is much more complex in the left hemisphere than in the right, the sagittal elements being more numerous and more branched than is common in the former hemisphere, and they tend to almost completely insulate portions of the brain substance.

Remarks on the Frontal Lobes.

(1) The general size of these lobes is about normally proportionate to that of the remainder of the hemispheres. Each hemisphere, however, is distinguished by the great breadth and complexity of its fronto-polar region in contrast to the condition of the subfrontal region which on both sides is partially defective and is relatively simple in pattern. There is now much evidence, to mention only that brought forward by Flechsig [11], Bolton [4] and [5], and Brodmann [6], to show that the latest regions of the frontal lobe to develop, both ontogenetically and phylogenetically, are the subfrontal and prefrontal.[1] In the cerebral hemispheres of the insane it is common to find one or other,

[1] *i.e.*, the prefontal in the meaning of Bolton and not in that of Brodmann.

or both, of these regions especially affected, either as a congenital defect, or as the result of loss due to cerebral wasting. In this particular specimen it is therefore of interest to note that whilst the prefrontal region is of great breath and is complex in pattern, the subfrontal is relatively defective and comparatively simply convoluted.

(2) The main sulci are for the most part deep, much curved, and possess many secondary spurs. The development of the sulci has proceeded on fairly regular lines and, as we consider, in the direction of superiority. The only definite tendency to insulation of portions of the cortex has occurred in the right orbital region. This tendency to the formation of islands of cortex either by branching and re-uniting of primary sulci or owing to the presence of unusual sulci, is looked upon by Mickle [15] as a sign of aberrant formative activity. As regards the external surface of the frontal lobes the left hemisphere appears to be slightly more complex in pattern than the right, although in places the latter is a little better convoluted than its fellow. With respect to the mesial and orbital surfaces of the lobes, the left side is decidedly superior to the right in convolutional complexity.

(3) The good development of the external sagittally coursing sulci, especially of the sulcus frontalis medius, which on the left side in this specimen is remarkably well formed for a *left* hemisphere, divides this part of each frontal lobe into four distinct, and for the most part, broad gyri. The superior of these is still further partially subdivided by branches of the sulcus frontalis mesialis which is also rather better developed on the left side than on the right.

According to Kohlbrugge [13] this four tier type of external frontal conformation is the common arrangement for the brains of Australians. Mickle [15] states that, found in some criminals, lunatics and mental defectives, it has been said to indicate marked aberrancy, Benedikt indeed believing that it is a sign of grave reversion to the four tier type of certain lower animals. Mickle himself, however, argues that, at least in many instances, this four (and five) tier type marks a higher than usual and not a lower brain formation, especially when due to division of the first frontal gyrus by unusual development of the s. frontalis mesialis. The same applies, although less convincingly, to the four tier form produced by marked development of the s. frontalis medius. The author quoted believes, contrary to Benedikt, that the latter is the more common arrangement, and this is in agreement with our own experience. The type thus formed has not infrequently been

seen in the larger cerebral hemispheres obtained at the Rainhill Asylum, and these hemispheres have, as a rule, belonged to people of originally good intelligence. Mickle, after concluding that instead of degradation and reversion, the four tier form must indicate in many cases a rather high position in brain evolution, remarks that, "this is indeed compatible with mental aberrancy, with unstable and labile mental activities, lively and powerful but not well directed—in a word, a brain function lacking in balance."

The Parietal Lobes.

The external surface.—The sulcus lettered M forms a fairly typical *s. subcentralis posterior* in both hemispheres.

The *sulcus post-centralis*. On the right side a series of sulci (o, o^1) make an almost complete boundary to the post-central gyrus, the annectants passing between this gyrus and the parietal lobules being narrow and mostly rather deep. In the left hemisphere the several elements of the post-central sulcus are for the most part widely separated from each other by broad superficial annectants. The superior branch (o) in this hemisphere shows the common arrangement of a stem bifurcating at its upper end to embrace the extremity of the s. cinguli (d). The sulci marked 21 and 29 in the right and left hemispheres respectively appear to belong to the post-central system, so that the inferior division of this sulcus is seemingly duplicated on both sides, as occasionally occurs. The furrows marked 20, 24 and 30 in the left hemisphere may perhaps be regarded as lateral branches of the s. post-centralis. The sulcus marked 20 on the left side (and more doubtfully that marked 15, 15, on the right) might be looked upon by some as constituting a form of *s. retrocentralis transversus* of Eberstaller, although rather shallow for this sulcus and placed somewhat high up in the hemisphere. Whatever name is given to this furrow there can be little doubt that, as Cole [8] has pointed out, a similar sulcus is of importance in the causation of the appearance of a large inferior Rolandic genu. Such a sulcus, as in this specimen, is usually better marked in the left hemisphere than in the right, presumably owing to the greater length of the posterior limb of the Sylvian complex in the former hemisphere.

The *sulcus interparietalis*. On the right side this consists of two independent portions, an anterior and longer (l) which is joined to a furrow taken to represent the middle part of the post-central sulcus,

and a posterior and shorter (*e*), the *pars occipitalis* or *paroccipital sulcus* of Wilder. Behind the latter is a well marked *s. occipitalis transversus* of Ecker (*m*, m^1). The sulcus numbered 25 in front of the sulci *e* and *m* may perhaps be regarded as a duplication of one or other of these furrows such as sometimes occurs in complex brains. In the left hemisphere the anterior division of the s. interparietalis is in two separate parts (*l*, *l*), the posterior of these being much shallower than the anterior. The posterior division of the sulcus *e* passes backwards and then rapidly downwards and backwards to join a typical s. occipitalis transversus (*m*, m^1). The branch marked 17 behind the latter may probably also be regarded as belonging to the *m* system.

From the upper side of the s. interparietalis in both hemispheres springs a well marked branch, the *ramus medialis primus* (T). The *ramus medialis secundus* (e^1) is short and deep, as is sometimes the case. It is typically placed on the left side, but is not so readily identified on the right.

From the under side of the *l* portion of the s. interparietalis in the right hemisphere arise three *rami ventrales* (*v*, *v*, *v*). The anterior of these is rather unusually well developed and forms a boundary between the supra-marginal and angular gyri. On the left side two ventral rami spring from the sulcus *l* and one from the sulcus *e*. The anterior of these in this hemisphere also is a long furrow.

The other sulci of this region can be more conveniently dealt with when considering the temporal lobes.

The mesial surface of the parietal lobes. Right hemisphere.—Whilst the posterior third of the precuneus is almost smooth, the anterior two-thirds are unusually complex. The lower sagittal division of the K system of sulci (the *s. subparietalis*) joins anteriorly the s. cinguli (see fig. 2*b*). The sulcus is much branched and cuts off the greater part of the precuneus from the gyrus cinguli.

Above this sulcus are two more transversely directed furrows (K27 and 17) such as one may find in this region. These may be regarded as *sulci præcunei*. The upper part of the anterior of the two sulci we think, however, forms a furrow which sometimes runs into or becomes a *sulcus parietalis superior* of Retzius. Reference is again made to this sulcus on p. 60.

Left hemisphere.—The precuneus is more simply and uniformly convoluted than on the right side. The branches of the K system are quite independent of each other and of other sulci. The two lower of these form a *sulcus subparietalis*, but broad annectants pass

between the precuneus and gyrus cinguli. The remarks made concerning the sulci K 27 and 17 of the right hemisphere apply also to the sulci marked K 33 and 25 (for sulcus 25 see fig. 4*b*) in this hemisphere.

The Temporal Lobes.

The superior surface.—On the right side one very long anterior transverse gyrus of Heschl is separated from two smaller posterior gyri by a deep sulcus, the outer part of which cuts into the greater part of the breadth of the first temporal gyrus. In the left hemisphere there are only two transverse gyri of Heschl, a long anterior gyrus separated from a shorter posterior one by a sulcus which indents the edge of the lobe.

The lateral and inferior surfaces. Right hemisphere. The sulcus temporalis superior, a.—This consists of two separate parts. The anterior of these is placed relatively unduly close to the edge of the lobe and is deflected in the hinder part of its course towards the Sylvian fossa, so that the anterior part of the first temporal gyrus is narrow. Occasionally this deflection of part of the superior temporal sulcus is complete, the branch turning right into the Sylvian depths. Such complete deflection, when present, appears to be much commoner on the left side than on the right. It is regarded by Mickle [15] as a departure from the usual, which, other things being equal, is in the direction of increased formative activity, and, although a deviation from type, is yet not necessarily a sign of inferiority. But there are other considerations which lead one to suppose that the condition may sometimes mean the persistence of an occasional fœtal tendency.

The posterior division of the sulcus is deep, and along its course several broad, deep annectants occur. It inclines away from the line of the Sylvian fossa, giving great breadth to the hinder part of the first temporal gyrus. This part of the sulcus sends off spurs upwards and downwards, and ends posteriorly in a bifurcation, forming a long anterior ascending limb (a^2) and a shorter posterior branch (a^1). The anterior branch, a^2, would probably be identified by Elliot Smith [10], and also by Kükenthal and Ziehen,[1] as the *sulcus gyri angularis*, although Zuckerkandl [25] (and also Bolk [3] for the gorilla) would regard the posterior branch a^1 as representing this sulcus. Kohlbrugge [12] and [13] does not name a determined furrow a sulcus gyri angularis. The reasons

[1] We have been unable to obtain access to Kükenthal and Ziehen's original work, and are only acquainted with their views in so far as they are discussed by the authors quoted.

for the identification of the anterior branch as the sulcus gyri angularis are, as Dr. Cole suggests, that it is the original continuation of the main part of the sulcus temporalis superior, and that it is found in the older cortex (in which the sulcus first appears) common both to apes and man, whereas the posterior branch is situated in, or near to, the newer cortex further back. As is well known, modern histological research has thrown much light on the order of development of the inferior parietal lobule, and the point above alluded to is but another illustration of the fact that the identification of sulci on the ground of mere topical considerations is apt to be fallacious.

The horizontally directed branches marked 12, a^1, and 15 may perhaps be regarded as forming a *s. parieto-temporalis* of Elliot Smith, partially separating the inferior parietal lobule from the temporal lobe.

The *sulci temporalis medius* (*i*) and *inferior* (f^1). The different divisions of these sulci have a fairly typical disposition, and are mostly separate from each other, although some of the posterior branches of the sulcus f^1 join to almost entirely insulate a considerable area of smooth cortex. In the more simply convoluted human brains the s. temporalis inferior is often closely associated with the s. collateralis—an indication of a reverting tendency. In this hemisphere these furrows are widely separated. The sulci of the lingual lobule are simple and shallow.

The sulcus marked *b* (also 19) appears to form a *s. occipitalis inferior* of Wernicke and Elliot Smith.

The *s. temporalis transversus* of Retzius, which commonly forms a fairly definite boundary to a distinct histological area (area temporopolaris (38) of Brodmann and of Elliot Smith), is represented by a posterior transverse branch of the anterior segment of the s. temporalis medius.

The lateral and inferior surfaces. Left hemisphere. The sulcus temporalis superior, a.—This sulcus is complex and is made up of several irregular branches, but the first temporal gyrus is of more uniform width than in the right hemisphere. The part of the sulcus behind and below the posterior Sylvian termination is broken up and is unusually shallow. Hereabouts also it joins with other furrows to almost entirely insulate a slightly depressed area of cortex. Behind this shallow split-up portion the sulcus divides into two terminal rami. The anterior of those a^2 may probably be looked upon as a *sulcus gyri angularis*. This sulcus is shallower than is the corresponding one of the right side, but it is longer and reaches to within about 20 mm. of the superior border of the hemisphere. The horizontal portion of the sulcus marked a^1 forms

together with the sulci lettered *b*, *b* a very typical *s. parieto-temporalis* of Elliot Smith, although the latter elements (*b*, *b*) may be regarded as a *s. occipitalis lateralis* of Eberstaller. The K shaped sulcus marked a^1 9, immediately above the posterior ascending terminal ramus a^1, appears to form a *s. occipitalis anterior* of Wernicke.

The *sulci temporalis medius* (*i*) and *inferior* (f^1). The branches of these sulci are fairly typically distributed, but are very numerous. Many are separate the one from the other, and are much forked and spurred, rendering on the whole the lateral and inferior aspects of the lobe markedly complex in pattern. One of the branches of the sulcus f^1 almost joins the s. collateralis. The *s. temporalis transversus*, apparently composed of transversely directed branches of the superior and middle temporal sulci, is more irregular than is the corresponding sulcus of the right hemisphere. The deep sulcus marked f^1 (also 45) is apparently a *s. occipitalis inferior* of Wernicke and Elliot Smith.

The Occipital Lobes.

The external surface.—The furrows of the mesial aspect of these lobes are fairly typical in distribution, but the arrangement of the sulci on the external surface of the lobes in this specimen, as is not infrequently the case, is not easily reconciled with any of the recognized descriptions of the sulci of this region. Dr. Kohlbrugge has been kind enough to letter the sulci of this region in these hemispheres according to the system used by him, and he has made the following observations:—

In every large brain a duplication of sulci may be seen, especially in the parietal and occipital regions. The sulcus *b* (which we have referred to as forming a *s. occipitalis lateralis* of Eberstaller) may be doubled in one or both sides. In this specimen the sulcus is tripled in each hemisphere. If the sulcus *b* is doubled the sulcus *x* is likely to be duplicated also, as in the right hemisphere in this case, the lower branch probably belonging to the *i* system (s. temporalis medius). In the left hemisphere this sulcus appears to be like a duplication of sulcus *b*. The sulcus *x* is also double and united with the *b* sulci in both hemispheres. The sulcus *u* is single on the right side but duplicated on the left. No sulcus which has the typical direction of a *s. paramesialis* is present in either hemisphere.

Remarks on the Parietal, Temporal and Occipital Lobes.

The general size of the parietal and temporal lobes of both hemispheres appears to be about normally proportionate to that of the

remainder of the hemispheres. The lateral surface of the occipital lobes, however, strike us as being relatively somewhat small in both hemispheres, although the latter well covered the cerebellum in the natural state. This relative smallness of the occipital lobes is by some regarded as an indication of good cerebral development, although, on the other hand, relative defect in size of these lobes is not infrequently seen in inferior brains.

The parietal lobes.—The post-central gyrus, especially in its upper and middle parts, is rather broader on the left side than on the right, and is more split up by cross sulci. This, however, is a common and presumably normal difference between the two hemispheres.

Owing to the different position in the two hemispheres of the component parts of the sulcus interparietalis and of the Sylvian fossa, there are certain differences on the two sides in the shape, and to some extent in the size of the superior parietal lobule and of the several parts of the inferior parietal lobule. But these differences are usual ones and doubtless quite within normal limits. Thus, whilst the supramarginal and angular gyri cover much the same extent of surface in the two hemispheres, on the right side the portion of the former gyrus in front of the posterior ascending Sylvian ramus is much narrower than is this portion in the left hemisphere, but the deficiency in this direction is mostly compensated for by an increase in height. The reverse applies, though to a less extent, to the angular gyrus, i.e., what this gyrus lacks in height in the right hemisphere is compensated for by increase in breadth. The post-parietal gyrus of the right hemisphere is distinctly larger in every direction than that of the left. The superior parietal lobule is of a very uniform breadth on the right side, but on the left lobule is broader in front and narrower behind as compared with its fellow of the opposite hemisphere.

It is of interest from the evolutionary aspect to note that the posterior part of the inferior parietal lobule—a region of the human brain which, according to Flechsig [11], is very late to myelinate, and which is relatively small in apes—is exceedingly well developed as regards size and complexity in both hemispheres, but especially so in the right.

The hinder part of the superior parietal lobule and of the precuneus appears to be large as compared with the fore part, particularly on the right side. This is also of developmental interest. As Cole [8] has pointed out, "the sulcus parietalis superior probably marks the boundary

between an area of earlier myelination in front and an area of later myelination behind. The area in front is a region which attains a high degree of development in the gorilla." In this specimen the anterior and superior sulci of the K system (K27 on the right side and K33 on the left) are probably the furrows partly separating these two areas, which, according to Flechsig [11], myelinate at different dates, as probably also they do the *area parietalis superior* B from the same named area A of Elliot Smith, regions which this observer [10] believes to be structurally distinct. In these hemispheres the region behind the sulci just referred to is of large size as compared with the region in front.

As regards their convolutional pattern the parietal lobes in general may be said to be markedly complex, and the sulci are for the most part developed on regular lines. Secondary spurs are numerous and many of the sulci are much curved, but some, especially of the inferior lobules, are relatively rather shallow. Attention has already been directed to the apparent duplication of certain sulci, particularly in the right hemisphere; in fact the latter hemisphere appears, on the whole, to be more complex than its fellow.

Duplication of the ordinary furrows Mickle [15] appears to regard as abnormal, as being indeed a perversion of developmental activity excessive in degree, but lower in kind or grade, ill-directed and aberrant. But it seems to us that if this duplication has occurred in a regular manner—as in most places in this specimen—it should be looked upon rather as a sign of superiority, especially as it is apt to occur in all hemispheres of a highly complex convolutional pattern.

The tendency to separateness of the different elements of the post-central and interparietal systems of sulci, especially on the left side, might be regarded by some as an indication of under persistence of fœtal characters owing to developmental failure, but judged by the context, i.e., by the complexity of the hemispheres generally, we consider that this should more probably be looked upon as a sign of increased formative activity in the direction of superiority.

In neither hemisphere is there any tendency to the formation of what Mickle [15] has termed a reversed occipital or posterior parietal operculum. This author regards such an appearance as a manifestation of over-activity on the part of the parietal with some relative defect of activity of the occipital region. The absence of such a formation in this specimen can probably be accounted for by the fact that the developmental activity of the occipital lobes, judging by the duplication of many of the sulci of their outer surface, has been as great, or almost as great, as that of the parietal.

The Temporal Lobes.

These appear to call for little comment. The different sulci are on the whole well developed, so that the several gyri are fairly distinctly marked off from each other. The left temporal lobe is decidedly more complex in pattern than the right, secondary spurs and forkings of the sulci being more numerous in the former hemisphere. This difference between the temporal lobes of the two hemispheres of the same brain is probably not uncommon.

The somewhat aberrant direction taken by the first part of the s. temporalis superior in the right hemisphere has already been mentioned.

There is an even more marked tendency to separateness of the different elements of the sulci of the temporal lobes than of the parietal lobes, and we think that the interpretation which was placed upon this in the instance of the latter lobes applies also to the former. At the same time we consider that there is greater irregularity and aberrancy of the sulci in the temporal regions, on the whole, particularly on the left side—as shown by the numerous spurs, forkings and tendency to insulation of areas of cortex—than occurs in any other part of the hemispheres.

The external parieto-occipital annectant gyri.—There is no clearly recognizable *sulcus lunatus* of Elliot Smith in either hemisphere, and sulci which may be regarded as homologous with an "affenspalte" are difficult to identify. In the left hemisphere, however, it may perhaps be said that the sulcus marked 17 and the anterior part of sulcus *b* bear a similar relationship to the *s. occipitalis transversus* to that which the "affenspalte" bears to this sulcus.

On the left side the course of the external parieto-occipital annectant gyri can be traced with some definiteness. The first annectant passes round the extremities of the ascending limb (m^1) of the *s. occipitalis transversus* and of the *parieto-occipital fossa*, and is bounded anteriorly by a short processus acuminis (e^1) and by the dorsal continuation of one of the *precuneal* sulci. The second annectant, superficial and of considerable size, forms a loop round the end of the descending limb (m) of the *s. occipitalis transversus*, and is bounded in front by branch of the sulcus identified as the *s. occipitalis anterior* of Wernicke (a^1 9). The third annectant passes across and around the anterior end of the s. occipitalis lateralis of Eberstaller (b) and is bounded anteriorly by branches of the superior and middle temporal sulci.

In the right hemisphere the course of the parieto-occipital

annectants is difficult to follow with any degree of certainty excepting that of the first which is a broad irregular gyrus passing round the extremity of the upper branch of the *s. occipitalis transversus* (o). But this gyrus is broken up by branches of the parieto-occipital complex and by sulci of the superior parietal lobule.

Zuckerkandl [25] has traced the course of the parieto-occipital annectant gyri in apes with much plausibility, but the attempt to identify these annectants in the human brain in every instance appears to us apt to lead to confusion. It seems by no means always clear which is which. In our experience the course of these annectants can not infrequently be more readily followed on the left side than on the right.

The insula; concealed areas of the frontal and parietal lobes. The limbic and olfactory lobes.—These parts, so far as can be seen without damage to the specimen, are, in both hemispheres, normally developed, have a size proportionate to that of the rest of the hemispheres, and show a convolutional pattern of at least average complexity.

Summary and General Remarks.

(1) The cerebral hemispheres are of good general shape, and the different lobes of each hemisphere appear to bear about a normal proportion to one another, excepting that the occipital lobes are relatively somewhat small. The subfrontal region on each side is also rather small and simply convoluted, but the deficiency of this region is relative only.

(2) The convolutional pattern of the hemispheres as a whole is exceedingly complex, and in the distribution of the several sulci little beyond the following has been detected which can be regarded as definite marks of inferiority. The right *sulcus collateralis* may be said to be defectively developed, and some signs of reversion or aberrancy are shown by the *calcarine* sulci, and perhaps by the right *sulcus cinguli*. There are tendencies to insulation of areas of cortex in the right orbital region and in the temporal regions; also to irregularity and aberrancy of the sulci in the latter regions, particularly on the left side. Some indications of defective formation or aberrancy of sulci, however, are to be found, we believe, in almost every human hemisphere, no matter how good the development in general may be. The duplication and triplication of the sulci such as occurs, especially in the occipital and parietal lobes in this specimen, we prefer to regard, for the reasons given, as departures in the direction of superiority.

(3) Many of the sulci are much curved, and on the whole they certainly exceed the average normal in depth, whilst having a depth which, for the most part, is normally proportionate to each other. In places, however, the sulci are somewhat shallow; e.g., some of the furrows of the left inferior parietal lobule, a portion of the left sulcus interparietalis, and the posterior part of the stem of the left sulcus temporalis superior.

(4) Certain differences exist in the convolutional pattern of the two hemispheres. These have been fully detailed in the foregoing pages, and we consider that in most instances they are only such as are very commonly found between two hemispheres of the same brain, and that probably they can be regarded as normal differences.

Part II.—Microscopical Examination.

The method of hardening the hemispheres employed and the reasons for this have already been stated. As it was desired to preserve one of the hemispheres as an almost complete museum specimen, the majority of the blocks for microscopical purposes were removed from the left hemisphere.

Sections, cut in paraffin, from the various regions were stained, after Nissl's method, with polychrome blue or thionin, and also for showing blood-vessels and neuroglia by the Heidenhain iron-hæmatoxylin method, followed by counter staining with eosin. The latter method fails to stain normal neuroglia fibrils—which is often an advantage—whilst giving an adequate display of all actively proliferating and abnormal neuroglia.

In all thirty-seven blocks were examined from the two cerebral hemispheres, twenty-nine from the left and eight from the right. It is unnecessary to detail the regions from which these blocks were removed, for the exact site of most of them is marked on the drawings (figs. 7 and 8) by a dotted line, against which a number is placed indicating the type of cortex found in the different situations. The numerals correspond to those used by Brodmann [6] in his map of the distribution of the histological areas of the human cerebral cortex.

The microscopical findings in this case are of interest from two separate points of view. Firstly, as an example of unusually large cerebral hemispheres, and secondly, as a case of epilepsy. From the latter aspect, the appearances which other observers, and particularly Turner [21], consider to be characteristic of epilepsy were carefully

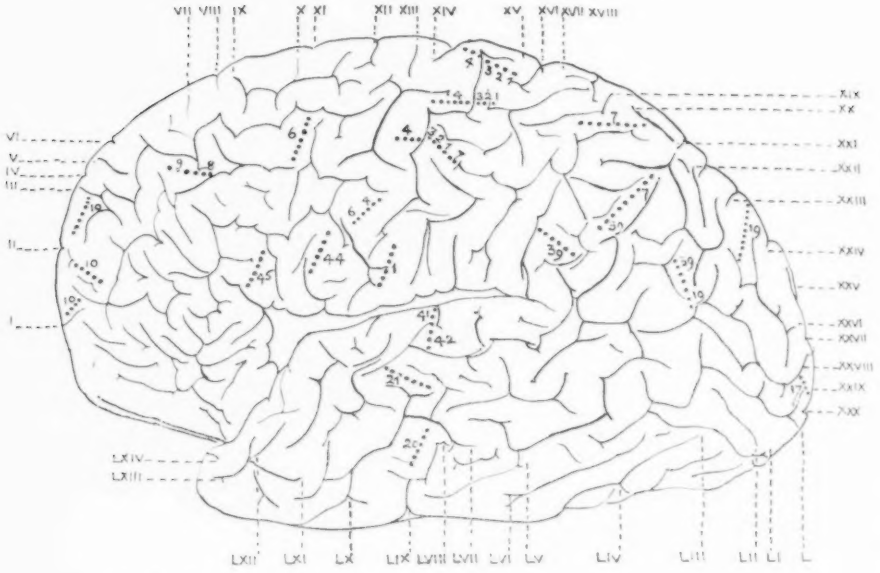

FIG. 7.—In this and the following figure the site of each of the blocks removed for microscopical examination is indicated by a dotted line. The numerals placed against these lines refer to the type of cortex found in the different situations, and correspond to those used by Brodmann for this purpose.

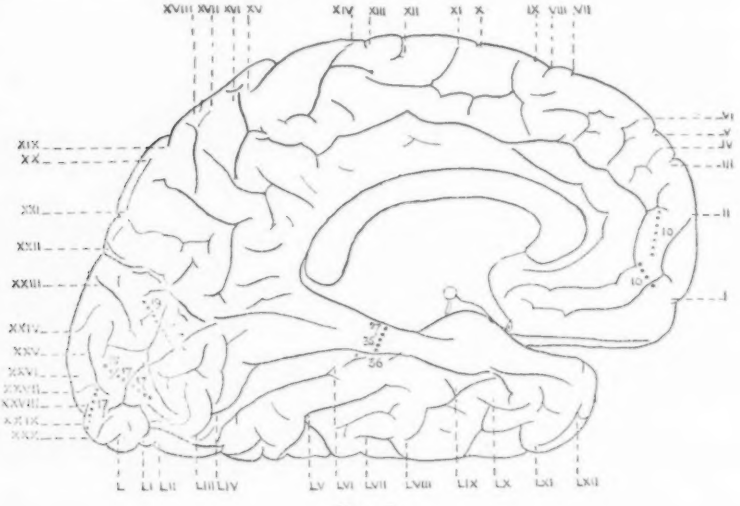

FIG. 8.

looked for during the examination of the sections. Allusion will be made to these in the course of the description which will be given under the following headings:—

(1) Types of cortex and their distribution.
(2) Structure of the cortex.
(3) Pathological changes.
  (*a*) The meninges.
  (*b*) The nerve-cells.
  (*c*) Gliosis and atrophy.
  (*d*) The blood-vessels—(i) structural alteration; (ii) perivascular and pericellular elements; (iii) congestion; (iv) intra- and extra-vascular clotting.

(1) *Types of Cortex and their Distribution.*

The different types of cortex found in all the regions from which blocks were cut are readily recognizable as usual to those regions, and in harmony with Brodmann's map of the distribution of the cortical fields of the human cerebral hemisphere, so that it may be said that the distribution of the different types of cortex in this specimen is normal, in at least so far as the hemispheres have been examined.

(2) *Structure of the Cortex.*

As regards its structure, the cortex of all the areas examined appears to be almost, if not quite, normal. The several laminæ of the cortex, so far as can be judged without micrometric measurement, are of good depth, and the individual nerve-cells are for the most part well formed. No cells were found in any region which could with certainty be described as under-developed, cells such as are commonly seen in cases of idiocy and imbecility. In the inferior parietal and middle temporal regions, however, the majority of the cells, particularly the smaller and medium-sized ones of the pyramidal layer, and many of those of the polymorphic layer, are somewhat globular or flask-shaped. As, however, degenerative change in the nerve-cells of those regions is considerable, it is impossible to state confidently that the shape of the cells, as above described, is due to congenital defect, and not to pathological alteration. At the same time it may be mentioned that, in our experience, under-developed cells are not infrequently met with in the brains of the insane in the inferior parietal and middle temporal regions, particularly in the latter.

The persistence of nerve-cells in the molecular layer, as seen by the

ordinary staining methods and the presence of subcortical nerve-cells, are conditions usually regarded as stigmata of defective nervous development. In this case the only situation in which definite nerve-cells can be recognized in the molecular layer—and they are few in number—is the *para-insular* region, and the only one in which subcortical nerve-cells are present in any considerable quantity is in the anterior part of the *area frontalis granularis*.

The nerve-fibres, even by such an imperfect method for their display as that of the iron-hæmatoxylin method of Heidenhain, are seen in abundance, and, excepting where associated with areas of local atrophy, they have an apparently normal appearance. In particular, it may be stated that the tangential fibres of the molecular layer exist in great numbers, especially in those regions such as the central gyri and parts of the occipital lobe where normally their presence is readily demonstrable.

(3) *Pathological Changes.*

(*a*) *The meninges.*—Owing to the membranes having been stripped before the blocks were removed, only small portions of these can be seen along the sulci in some of the sections. When present, the meninges show considerable congestion, some fibroid thickening, and small-cell infiltration, but no hæmorrhages. A small amount of amorphous epicerebral exudate was found below the pia in one section from the left occipital region.

(*b*) *The nerve-cells.*—The nerve-cells show more or less marked degenerative changes, chiefly of a chronic nature, in the majority of the regions examined. With the exception of the Betz-cells of the precentral gyrus and the cells of the cornu ammonis, to which special reference will be made later, the cells most affected are the smaller, and to a less extent the medium-sized cells of the pyramidal lamina, although in places many of the cells of the polymorphic lamina are swollen and vacuolated. Nowhere, however, is any great loss of cells apparent excepting in a focus of atrophy in the post-central gyrus. The changes just mentioned, although not anywhere very marked, are most prominent in the following regions: the mid-frontal gyrus (*area frontalis granularis*); the inferior frontal (*area opercularis*); the middle and inferior temporal areas. They are next most marked in the prefrontal region (*area fronto-polaris*); the inferior frontal (*area triangularis*), and remainder of the frontal lobe examined including the precentral gyrus, and in the inferior parietal area. They are least evident

in the various parts of the occipital lobe, in the post-central gyrus, in the gyrus of Heschl and superior temporal area, and in the para-insular and ectorhinal areas; in fact, the nerve-cells in many sections from the several last-named regions may be described as almost normal in appearance. It is of importance to note that in all parts where the nerve-cell changes are most marked, these changes are generalized rather than focal in nature, excepting in the area of atrophy of the post-central gyrus, to which allusion has been made. In certain parts where spaces exist between the nerve-cells, which might possibly be mistaken for areas of loss of nerve-cells, such spaces are normal to the type of cortex found in this particular region.

The Betz-cells.—These in all parts of the precentral gyrus examined are affected, and more so than the cells of the other laminæ of this region. Few, if any, of the hundreds of cells examined can be said to be normal; all show, at least, some chromatolysis, and great numbers of them have reached an advanced stage of degeneration. Many of the cells are swollen, whilst others are shrunken and are deficient in processes. Some cells stain deeply and diffusely, so that no definite chromophile elements can be distinguished. In the majority of the cells, however, the stainable substance is very deficient; the chromatolysis is sometimes diffuse or central, but in most cells it is of the axonal type. The nucleus of the cell is in some instances swollen, but more often it is shrunken; frequently it is displaced, and in many cells partially extruded. In view of the fact that the patient suffered from epilepsy, it is of interest to specially note that the affection of the Betz-cells is much greater than is that of the homonymous solitary cells of Meynert, in other regions which are for the most part practically normal in appearance.

(c) *Gliosis and atrophy.*—Sclerosis of the outer layer of the cortex is regarded by Bleuler [2] as characteristic of epilepsy, and in fact as an essential factor in the pathology of the disease. In this case a small amount of subpial neuroglial felting, forming a thin surface rim, is present in all the regions of the cortex examined, being most evident in the cornu ammonis and neighbouring subicular region, in the gyrus of Heschl, and in the para-insular region. In some parts also a few—usually a very few—proliferating glia-cells can be seen in the zonal layer. At no other level of the cortex, and in no part of the white matter in any region of the neopallium examined is there any definite proliferation of neuroglia, unless the moderate increase of the elements described below as "perivascular" and "pericellular" can be so regarded.

Turner [21] states that in none of his cases of epilepsy was the glial increase considerable—not indeed greater than is usual in cases of chronic insanity—and, if the cornu ammonis and gyrus dentatus be excluded, the same may be said with regard to this specimen.

The cornu ammonis.—Sclerosis of the cornu ammonis is regarded by many as highly characteristic of epilepsy (Worcester [24], Turner [21]). Turner found this condition in 48 per cent. of his cases, and he states that the microscropical appearances are chiefly of a negative character. "There is no increase of glia, the nerve-cells are few in number, and those present are generally degenerated, the vessels lie in wide lymph spaces and are collapsed and atrophied, or may have undergone hyaline degeneration. Small hæmorrhages are generally found in the cortex."

In this case the cornu ammonis appeared to the naked eye to be normal in both hemispheres. Only that of the left side was examined microscopically, and in this a very definite lesion was found, which, however, differed in appearance from that described by Turner [21]. In the cornu ammonis, gyrus dentatus, and to a less extent in the subiculum, there is below the condensed surface rim of glia already alluded to a marked generalized proliferation of glia near the surface and extending to a considerable depth, but there are no surface granulations. In addition to this, but separated from the more superficially proliferating glia is a deeper and extensive area of gliosis involving the greater part of the cornu ammonis and gyrus dentatus. In this area glia-cells are seen in all stages of formation. Most of them are giant cells, some with a large amount of lightly staining cytoplasm and with processes in various stages of condensation, others with a little darkly staining cytoplasm and numerous darkly staining processes. The glia-cells are massed chiefly around the blood-vessels and many processes are seen passing from them to the latter. The area appears to have started from several distinct foci. The nerve-cells of the stratum granulosum and stratum pyramidalium are in abundance, and although many of these are degenerated, they do not appear to have suffered any actual loss. The blood-vessels are not collapsed but well fill the lymph spaces, which are nowhere dilated. The vessel walls show only a moderate amount of hyaline degeneration and thickening. There is much congestion of the vessels, but there are no signs of intravascular clotting and no hæmorrhages. The condition is a definite gliosis, possibly following minute softenings, but of the latter there is no present evidence.

Several small areas of atrophy with little or no active gliosis are

present. The largest of these is in the post-central gyrus near the top. It is an irregular wedge-shaped area involving all the laminæ of the cortex down to and including the granule layer. The atrophic patch contains a few scattered and stunted nerve-cells, and the lamination on either side of it is much disturbed, but there is little glial or vascular proliferation. Another area of atrophy was found in the precentral gyrus near the top. This is situated in the white matter and shows spaces crossed by swollen and varicose nerve-fibres. Other small areas of apparent atrophy without gliosis are seen in the white matter of the post-central gyrus, mid-temporal and prefrontal regions, but most of these are so minute that the possibility of their being artefacts cannot be altogether excluded.

(*d*) *The blood vessels.*—(i) *Structural alteration.*—There are no signs of endarteritis and the capillaries are practically normal. The only distinct change is some thickening and hyaline degeneration of the (microscopically) larger vessels. This varies considerably in different regions; it is usually slight and nowhere very marked. The vessels of the inferior parietal region are more affected than those elsewhere, not even excepting the cornu ammonis, and those of the right prefrontal region are rather more involved than those of the left.

(ii) *Perivascular and pericellular elements.*—The small perivascular elements are in general moderately increased in number. They adhere to the distal wall of the lymph spaces and are of various forms and staining reaction. Some appear to be lymphocytes and others, showing traces of cytoplasm, are probably neuroglia-cells, and possibly, as Turner [21] believes, mesoglia-cells of Ford Robertson. These elements are most numerous about the medium-sized vessels of the white matter and least prominent about the capillaries. There are no plasma-cells. The pericellular elements appear to be of a nature similar to the perivascular, and whilst nowhere very numerous, are most conspicuous in those regions showing the greatest amount of degeneration of the nerve-cells.

(iii) *Congestion.*—The veins and capillaries are intensely congested in most of the regions examined, but least so in the occipital region. The capillaries, owing to their engorgement, seem more numerous than normal. The distended veins, for the most part, completely fill the lymph spaces, but no varicosity was noticed. One or two minute capillary hæmorrhages were found in one block from the precentral gyrus.

(iv) *Intravascular and extravascular clots.*—In view of the important rôle which Turner [21] believes these clots to play in the causation of epilepsy, they were looked for with special care. Turner's thesis is that

"epilepsy is a disease occurring in persons with a defect of the nervous system, either congenital or involutional, in whom also there is an abnormal state of the blood, characterized by a special tendency to clotting; and that the fits . . . owe their exciting cause to sudden stasis of the blood-stream in some (generally limited) portion of the cortex, resulting from the blocking of cerebral cortical vessels by these aforementioned intravascular clots."

Clots having features similar to those described by Turner as occurring with such frequency in epilepsy, and which he believes to be the result of a vital process, were found in some vessels in many of the regions examined. No fibrin formation was seen in any of the vessels, the clots taking the form either of minute round deeply staining granules or of larger, more or less spherical, hyaline bodies, or again of a finely granular fainter staining débris, sometimes immediately outside the vessels. The thrombosis, however, as seen by the staining methods used, was not anywhere very marked. In a given section from many of the regions perhaps only one or two vessels showed any evidence of intra- or extra-vascular clotting, and often this was slight. No thrombi at all were seen in or around the vessels in sections from the following regions; three out of five blocks from the left prefrontal region, the block from the anterior part of the area frontalis granularis, that from the upper part of the post-central region and all the blocks, excepting one, from the occipital and pre-occipital regions of both hemispheres. The clotting is slight but distinctly evident in all sections from the parietal and temporal regions excepting the middle temporal, where it is a fairly prominent feature. The vessels showing the greatest amount of clotting are, on the whole, those of the precentral gyrus, but even here much variability exists in different parts. The thrombi are more numerous in the vessels of the white matter than in those of the grey. On reference to the account of the regional distribution of the nerve-cell degeneration (see pp. 66, 67), it will be observed that there is no constant relationship between the severity of such degeneration and the amount of intravascular clotting as seen in the sections.

Summary of the Microscopical Appearances and Remarks.

(1) The presence of a considerable number of subcortical nerve-cells in the anterior part of the area frontalis granularis, and of a few nerve-cells (seen by ordinary staining methods) in the zonal layer of the para-insular region, together with the somewhat more doubtful existence

of under-developed nerve-cells in the inferior parietal and mid-temporal regions, are the only evidences found of defective nervous development.

(2) Otherwise the cerebral hemispheres, so far as examined, appear in every way to be normally constituted, and their great size and weight cannot be accounted for by the very slight increase in neuroglia and thickening of the vessels which existed.

(3) Certain abnormalities were found, however, which are obviously the result of pathological change.

(*a*) The lesion of the Betz-cells is remarkable in that almost all the cells examined are more or less profoundly affected, in great contrast to the condition of the great majority of the homonymous solitary cells of Meynert in other regions. The presence of an immature form of Betz-cell, characterized by its similarity to that seen in an early stage of axonal degeneration, is regarded by Turner [21] as an expression of congenital defect of the nervous system, which is of primary importance in the etiology of epilepsy. In our experience Betz-cells, either of an axonal type or otherwise congenitally defective, are almost constantly found in the precentral gyrus of idiots and low grade imbeciles, whether the patients have suffered from epilepsy or not. But it may well be that in this case, and probably in other cases of epilepsy occurring in subjects whose brains are apparently not at all, or only slightly, congenitally defective, the appearances seen in the Betz-cells are of a degenerative nature, the result of prolonged exhaustion occasioned by the epileptic discharges. One of us at least (J. W.) inclines to the view that the *fons et origo* of epilepsy must be sought for in the instability, and consequent loss of control, on the part of the higher motor nervous arrangements rather than in the congenital defect of the Betz-cells themselves.

(*b*) Other morbid changes, particularly in certain areas, and affecting especially the smaller and medium-sized cells of the pyramidal layer, are present, but these appear, for the most part, to be the expression of a generalized degeneration process rather than focal lesions due to local vascular occlusion. A certain number of limited areas of atrophy, however, do exist—one in the grey matter of the post-central gyrus and others in the white matter of various parts—but these, although of interest as local changes, are not numerous, considering the number of sections examined, and as compared with their frequency in the cases of epilepsy described by Turner [21].

(*c*) Apart from the area of pronounced gliosis found in the cornu ammonis the amount of glia proliferation is not greater than that commonly seen in cases of chronic insanity.

(*d*) Evidences of intravascular and extravascular clotting exist in many of the regions examined, but no definite correlation between the extent of this and the amount of neuronic degeneration could be determined.

Part III.—General Remarks and Conclusions.

The pathology of hypertrophy of the brain appears to be very imperfectly understood, and there seems to be little object in discussing the matter fully here, as in this case nothing has been found which throws light on the subject.

Cases of so-called cerebral hyperplasia may be divided into at least two distinct classes, unilateral or localised and general.

Apparently four cases of hyperplasia of one cerebral hemisphere have been recorded, notably one by Douglas Webster [23], who gives an account of the literature of the subject generally, and to whose paper we are indebted for some of the following particulars:—

In Webster's case there was also unilateral hypertrophy of the body and an acromegalic condition of the feet. Numerous glia-cells were found in the left insular region of the brain, one of the specially hypertrophied parts, and the left cerebral hemisphere was as a whole more richly vascularised than the right.

In a case reported by J. Batty Tuke [20] there was co-existent atrophy of the left side of the body and considerable glial increase especially in the left occipital lobe of the brain.

Our case falls into a different category and appears more closely to resemble an instance of general hypertrophy of the brain, recorded by Anton [1], in which few or no pathological changes were found apart from those usually associated with epilepsy.

Various conditions have been assigned a causal relation to the cases of cerebral hyperplasia reported. Amongst these the following appear to be the most important, although trauma, lead-poisoning, enteric fever and rickets have also been discussed.

Heredity, as in van Walsem's [22] case of an epileptic idiot, aged 21, who had two macrocephalic brothers.

Hydrocephalus: an acute hydrocephalus is suggested as a possible cause of the hypertrophy in Tuke's case.

Disturbances of internal secretion: Anton [1] discusses the relationship of the adrenals to cerebral malformation, but these organs, examined microscopically in Webster's case, appeared to be normal, as also was

the hypophysis cerebri, except for some increase of the chromophile cells.

Hyperæmia: Webster [23] suggests as a more probable cause in his case vasomotor disturbance of one side of the body, particularly of the internal carotid artery and its branches.

Cases of very pronounced macrocephaly are of such comparative rarity that we think the record of our case may prove of interest even though the origin of the matter still remains obscure. None of the conditions which have assigned a causal relationship in this connection appear to have been present. The internal secretory glands were unfortunately not preserved for microscopical examination, but to the naked eye these all seemed to be quite normal.

The brain, although one of the heaviest on record, is, as will have been gathered from the detailed description, for the most part normal in appearance differing from the average brain mainly in its increased size and complexity of pattern. The microscopical changes found also do not at all necessarily bear upon the question of cerebral hypertrophy, being merely those usually present in the brains of chronic epileptics. On one point, however, the microscopical examination gave definite, although negative, results. There is no general hyperplasia of the neuroglia such as has been considered to form the basis of the cerebral hypertrophy in some cases.

Although there are some indications in places of defective development of the sulci and of reverting tendencies, these are not numerous, nor are they pronounced, probably not more so than are such indications in the majority of human brains, even in those which may be described as generally well developed.

There are, however, in the cerebral hemispheres many signs—apart from their large size—of a formative activity much greater than that usually seen. But we think that this increased developmental activity has proceeded, for the most part, on regular lines, and that on the whole the departures from the ordinary in the convolutional pattern of the brain are in the direction of superiority. On the other hand, the tendency to insulation of areas of cortex, and the marked spurring and forking of certain sulci, such as is seen particularly in the left temporal region, may probably be looked upon as indications of formative activity on irregular or aberrant lines. With this greatly increased developmental activity, whether in the direction of superiority or of aberrancy, it seems likely that there would be a tendency to instability.

It is of interest to note, in this connection, that unlike many other

recorded cases of this class, the patient was neither idiotic nor imbecile, but was originally of at least average general intelligence, with special ability in music. Epilepsy, as in this instance, is a frequent complication of these cases, and this suggests the idea that even when the minute structure of the brain appears to be normally constituted—which it by no means always is in such cases—the usual size of the brain, apart from its increased complexity of pattern, cannot be largely exceeded without introducing a condition of instability which renders its possessor liable to suffer from some form of nervous breakdown, and especially from epilepsy.

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THE RELATION OF THE MYOPATHIES.[1]

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THE classification of the myopathies is no easy task, but we may recognize two great groups of muscular atrophy or arrest, (1) the congenital, (2) the acquired.

The congenital embraces the cases of arrested growth in certain limited regions of the body, the infantile nuclear arrest ("Kernschwund") of Möbius. This muscular condition may be caused by defect of muscles with complete integrity of the nerve apparatus, or, on the other hand, the peripheral neurones may be much affected. The congenital arrest usually is not progressive, although it may be progressive in exceptional cases.

The acquired muscular atrophy also consists of two types, the primarily muscular, with intact nervous system, and the nuclear (neuronic), in which the nerve-cells of the peripheral neurones are affected. In the former we have the progressive muscular dystrophy, including the bulbar form of Hoffmann; in the latter we have the Werdnig-Hoffmann muscular atrophy, the infantile bulbar atrophy of Fazio, Charcot, and Londe, and the forms of myelopathy occurring later than the period of childhood. These types, as is well known, are progressive.

The various forms are combined in rare cases, and certain of the muscles of the body, as the pectorals and serratus magnus, show a special liability to arrest or atrophy in both forms. It is also well known that reaction of degeneration and fibrillary tremors, as well as changes in the cells of the anterior horns, have been observed in progressive muscular dystrophy, so that sharp distinctions cannot invariably be maintained.

The relation of muscular defect to progressive muscular dystrophy has been recognized by a number of investigators. By some the defect

[1] This paper was laid before the Neuropathological Section of the International Medical Congress [August 9, 1913].

has been considered as arrested intra-uterine dystrophy. In persisting portions of arrested muscles the histological findings have been those suggesting intra-uterine muscular dystrophy, and yet one must be cautious in accepting these findings as conclusive, for it is questionable whether a decision can be formed as to the myopathic or myelopathic character of atrophy from the microscopical findings in the muscles alone. In a paper published in 1898, and in another published in 1900, I called attention to the fact, even at that time well known, that the distinctions which had been sharply drawn between "degenerative" and "simple" muscular atrophy were not trustworthy, and that the histological investigation of the muscles could not determine the myelopathic or myopathic nature of the atrophy [52]. Combinations of muscular defect with muscular dystrophy have been described.

Recently we have had the classification of myopathy considered in an able article by Frederick E. Batten [3]. His classification affords an excellent basis for discussion. It is as follows:—

(1) The simple atrophic type (myatonia congenita or amyotonia congenita).

(2) The pseudo-hypertrophic type.

(3) The juvenile type (Erb).

(4) The facio-scapulo-humeral type (Landouzy and Dejerine).

(5) The distal type (Gowers).

(6) The myotonia atrophica type.

(7) Mixed and transitional types.

To these I add a somewhat questionable type:—

(8) The true hypertrophic type.

I shall have little to say regarding the types mentioned in the headings 2, 3 and 4; they have been the subject of innumerable papers by Duchenne, Erb, Landouzy and Dejerine, and a host of others. Their sharp limitation, however, is still a matter of dispute, and among recent writers on this subject may be mentioned Eulenburg and Toby Cohn [25]. These authors show by the report of five cases of dystrophy in one family that it may be impossible to class a given case under any one of the recognized types. They maintain that the types are useful for didactic purposes, but should not be too sharply insisted on, and with this view we must agree.

The simple atrophic type, as described by Batten, is one of the most disputed. It is congenital or begins in early infancy, and is characterized by smallness, lack of power and loss of tone in all the muscles of the body, without localized atrophy or hypertrophy of individual muscles

or groups of muscles. All movements are performed in a feeble manner. The disease is slowly progressive, and, as a rule, walking is never learnt. The muscles are very flaccid, and the hands and feet can be bent at unusual angles to the arms and legs. Some contractions of the flexors take place late in the disease. With this type Batten assimilates amyotonia congenita, and unquestionably there are many points of resemblance. The distinctions, as Collier and Wilson [14] formulate them, are:—

(1) The myopathies are conspicuously familial diseases, whereas no familial tendency has been recorded in amyotonia.

(2) The several types of myopathy often show familial relationship one with another, whereas no case of amyotonia has been reported in the myopathic family.

(3) A large majority of the cases of amyotonia are congenital, the condition being obvious at birth. In a minority of cases amyotonia has appeared acutely and has reached its most severe degree in a few days. In none of its several types is myopathy present at birth, nor does it ever appear acutely or reach its maximum in a few days.

(4) The characteristic muscular flaccidity is not present in myopathy.

(5) The local muscular wasting that is a marked feature of myopathy is not present in amyotonia.

(6) The course of myopathy is one of progressive muscular weakness, that of amyotonia is one of progressive amelioration of the symptoms.

(7) Return of the deep reflexes after their persistent absence for months or years has been recorded several times in amyotonia, and has occurred in two of the cases reported by Collier and Wilson. Such a return of an absent deep reflex has never been recorded in myopathy.

To these distinctions we may add two presented by Collier and Holmes, viz.:—

(8) Affection of the periphery of the limbs, and especially of the intrinsic hand muscles, which is the invariable rule in amyotonia, is of the greatest rarity in any form of myopathy.

In comparison with this positive statement, Archangelsky and Abrikosoff assert that the feet and hands in amyotonia usually are affected in less degree than the central portions of the limbs.

(9) Amyotonia never spreads to regions previously unaffected. Slow spreading of the affection from muscle to muscle is characteristic of all forms of myopathy.

Batten attempts to show that amyotonia may be a family disease, and in support of this argument he refers to the two cases of amyotonia in children of one family reported by Sylvestri. He refers also to the three cases in one family recorded by Finkelnburg, in one of which a pathological examination was obtained. He adds that one of the children, D.S., recorded by himself as having the simple atrophic type, had a younger brother similarly affected, although at the time of publication he was ignorant of this. These facts, Batten thinks, dispose of the first two points raised, viz., they demonstrate that amyotonia may be a familial disease and may occur in a myopathic family.

Cassirer [11] does not regard the cases of Finkelnburg in discussing the familial occurrence of amyotonia congenita, and states that only Sorgente and Beevor have described cases occurring in the same family, and these, he thinks, are questionable cases. He refers, however, to Sylvestri's cases which presented the characteristic symptoms of the disease, but regards them as uncertain. Further in his article Cassirer speaks of the familial form as described by Collier and Wilson, but regards all cases as "nicht ganz einwandfrei." It may be well to make a brief reference to these cases here.

Batten gives Sylvestri's cases as follows: S. recorded two cases of amyotonia in one family, the first and fifth children; the second and third being healthy, the fourth being a cretin. A maternal aunt suffered from the Landouzy-Dejerine form of myopathy. The elder child, at the age of 16, is said to have presented a typical picture of Erb's juvenile form. Sylvestri's description of the later development of this child is somewhat obscure.

Sevestre's [51] cases: A child, aged 2½ months, had from birth flaccid paralysis with atrophy of the four limbs and trunk, except the diaphragm. Two other children in the family had a similar disorder. The paralysis was almost complete.

The cases of Sorgente, brother and sister, as given in abstract by Collier and Wilson, presented the symptoms of amyotonia, and apparently nothing contrary to the complex, unless possibly that there was no reaction in muscles of the legs to either faradic or galvanic current, and convulsions occurred before death. These were familial cases, and were without necropsy.

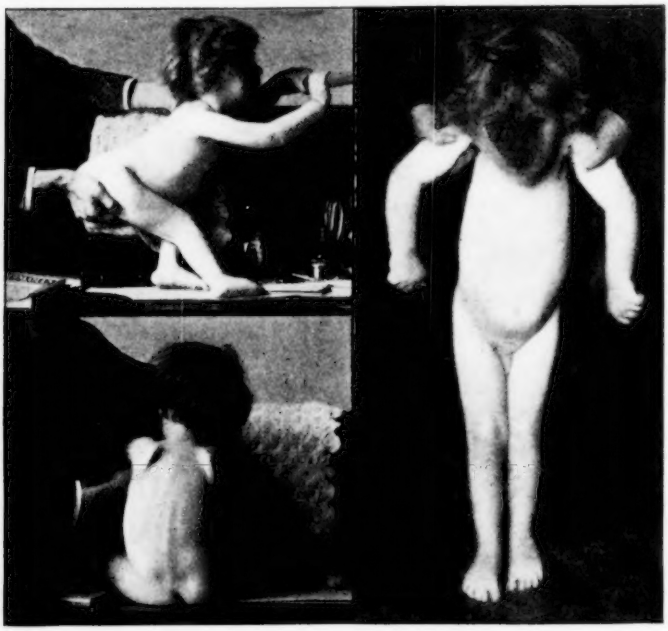
The case that Beevor described in BRAIN, 1902, was regarded by him as belonging to the Werdnig-Hoffmann type. It differed from this in that sensation was entirely abolished to the level of the second

rib, and also in the age at which the symptoms began. The condition developed *in utero*, and the child died when it was nine weeks old, so that the disease in this family began earlier and was very much more rapid than in other recorded cases. Pathologically, the case was like the recorded cases in that the cells of the anterior horns were extremely atrophied, but it differed from them in that the posterior columns were degenerated. Other children in the family were affected.

The paper of Finkelnburg [26] makes the resemblance of certain cases of amyotonia, such as those of Spiller, Lereboullet and Baudouin, and Councilman and Dunn, to muscular dystrophy striking. As Finkelnburg says, in spite of the immense amount of work done regarding muscular dystrophy, anatomical investigation of cases in the first months of life did not exist previous to his study. A microscopical examination of dystrophic tissue in early life, he thinks, is of great value in the disputed question of neuropathic or myelopathic nature of the disorder. His case was as follows: A boy, aged 21 months, developed normally until the eleventh month, according to the mother's statement. He could sit alone at the sixth month, and attempted first to stand at the ninth month. At the eleventh month the mother noticed the child had lack of muscular tonicity. In sitting he sank forward, so that he must be held by the shoulder-girdle. One can hardly suppose from these statements that the child was normal until he was 11 months old; such weakness would be gradual in development. The disease must have been congenital or acquired in the first months. The calf and gluteal muscles were especially well developed, although very soft, in contrast with the atrophied upper arm and shoulder muscles. The limbs were weak, especially in the proximal parts. The tendon reflexes of the lower limbs were not obtained. The child lived only three days under medical observation. Two other children in the family had muscular dystrophy at the eighteenth and twenty-fourth month respectively. Carey Coombs's case of amyotonia is interesting in this connexion inasmuch as the upper limbs were more affected than the lower.

In this case of Finkelnburg there is much to suggest amyotonia from a clinical point of view. The findings suggested muscular dystrophy, but there were, on microscopical examination, fields composed entirely of very small muscle-fibres without increase of connective tissue between them. Finkelnburg thought these small fibres could not be considered as normal fibres in a state of development, as they were much smaller than they should be in a child of the age of his patient.

Councilman and Dunn, however, have shown that muscle-fibres vary greatly in size in children of the same age. Finkelnburg concluded that the small fibres were not atrophied fibres, but fibres arrested in their development, and their tendency to dystrophic change was shown in the presence of hypertrophied fibres among the small fibres. No changes in the nerve-cells were found.



FIGS. 1, 2, and 3.—Congenital weakness and hypotonia with "winged scapulæ" and "loose shoulders."

Dr. Langley Porter, of San Francisco, California, has given me the notes of a very interesting family in which the diagnosis between amyotonia and muscular dystrophy is not altogether easy. The disease is a familial one.

The parents of the children are healthy, and no similar disease is known in the ancestry. A maternal grandfather had syphilis. The family consisted of five children. The first child, a girl, is now aged 14, well developed and normal. The second child, a boy, had a condition which may have been amyotonia or muscular dystrophy

with rickets. He had recurrent attacks of bronchitis, and died in one of these. He was never able to sit erect, to hold the head erect, or to raise the upper limbs above the shoulders. No electrical reactions were taken. The third child, a girl, now aged 9, is in perfect health. The fourth child, a boy, died a few days after birth, and possibly had an atonic condition. The fifth child, a boy, is now aged 3 and a few months (April, 1911), figs. 1, 2 and 3. He did not use his hands as infants do; he fixed his eyes on objects, but did not reach out to grasp. He did not hold up his head until he was more than a year old. He was not able to sit erect until he was 20 months old. He has never shown any inclination to stand. When 14 months old, he did not use his hands well; now he uses them very well. He has no power in the shoulder-girdle, and the muscles of this part, the erectors of the spine, and all the nucles of the hips and thighs are small, so that all these groups appear smoother and flatter than normal, though not distinctly atrophied. He has distinctly "winged scapulæ" and "loose shoulders." He can flex the feet to a right angle and move the toes freely. He sits on the buttocks and twists himself from side to side in moving over the floor. Hypotonicity is pronounced, so that the front of the thighs can be placed against the trunk. The boy is very intelligent.

In a letter received from Dr. Porter nineteen months after the above notes were taken, it is stated that the boy has shown steady improvement in power of all the muscles other than those of the shoulder and hip-girdle groups, and of the neck. He still has difficulty in supporting his head, especially when he loses its balance, at which time it drops on to the chest, but never rolls sidewise nor backward. He can hold himself erect if supported by leaning against some object, but has no power to stand independently. He is subject to frequent attacks of bronchitis, and it is evident that the respiratory musculature is weakened.

The weakness in this case was congenital; this fact and the progressive improvement convinced Dr. Porter that the case is one of amyotonia, notwithstanding the familial character of the disease. On the other hand, the marked weakness of the muscles of the shoulder-girdle, the winged scapulæ and loose shoulders are suggestive of muscular dystrophy. Remarkable for dystrophy is the congenital commencement and the hypotonicity, so great that the front of the thighs can be placed against the trunk. Whatever view may be entertained regarding this interesting family, it shows clearly that a diagnosis between amyotonia and dystrophy may be difficult.

It thus appears that it is impossible to maintain that in amyotonia there is:—

(1) Absence of any familial tendency in the incidence of the disease.

(2) Absence of any familial or ætiological relation with myopathy.

The question now to be answered is: Are there any cases of myopathy in which the disease was present at birth?

If Dr. Porter's case be one of myopathy, as I am inclined to believe, the answer to this question is in the affirmative. Finkelnburg's case was one of very early myopathy, and possibly earlier than is recorded. Kaufman Schlivek [49] reports a case of congenital myopathy. The anterior part of the arms was flat, soft, and flabby. The posterior part was better developed, but also soft and flabby. The shoulders and forearms were well developed. Active motion was limited at the shoulder; pronation and supination of the forearms was good. Motion in the wrists, hands, and fingers was normal. The muscles of the thighs and legs were soft and flabby. There was lordosis when the child stood, but not when she was sitting. Knee-jerks were present. Electrical reactions showed only quantitative change. The author considered and excluded amyotonia.

Russell Howard [37] reported a case of congenital defect of the muscular system (dystrophia muscularis congenita), and its association with congenital talipes equino-varus. The child was one of twins, and lived seven days. The report is a pathological one. The spinal cord was not examined microscopically, but peripheral nerves were examined, and were normal. The case was regarded as one of primary degeneration of the muscles occurring before birth. The writer believes congenital talipes may be a limited congenital muscular dystrophy.

It is doubtful whether either amyotonia or myopathy ever begins acutely or reaches a maximum within a few days. Batten thinks a development of this kind is rare, and the cases in which it has been recorded can hardly be taken as proof of its occurrence. He gives no references to any cases of this character, and states that it is admitted that an acute illness may bring into prominence symptoms which have not been observed previously; but it has not been proved that the true hypotonic condition of the muscles seen in typical cases of amyotonia is acutely produced.

Collier and Wilson, [14] however, assert that in three cases the condition came on rapidly, and reached its maximum within a few days of the onset of an acute illness in a previously healthy child. In one of their cases an attack of acute bronchitis was followed by complete

paralysis within a week in a child aged 12 months, who had been until this time apparently healthy. In Leclerc's case a healthy child, aged seven weeks, was seized with broncho-pneumonia, and became paralysed generally within a few days, and though slow improvement had gone on all the time, four years later the case was typically one of amyotonia. In Comby's case the amyotonia came on rapidly, following an attack of diarrhœa at four weeks, and was almost universal in its extent, and severe in degree. Collier and Wilson say the histories of these three cases hardly admit of the explanation, that we are here dealing with the effect of an acute illness in bringing into evidence an amyotonic condition already present in minor degree, but it suggests strongly that an acute toxic process was the cause of the amyotonia.

Leclerc [41] was doubtful of the correctness of the parents' statement concerning the rapidity of the onset. He says the child appeared normal at first, but at the age of seven weeks had broncho-pneumonia and spasm of the glottis, and the muscular condition then developed. He asserts, however, that it was a typical case of amyotonia, that it was almost certainly congenital, even through the parents believed the spasm of the glottis indicated the onset of the amyotonia. He thought the parents overlooked the early condition. At all events, the increase of the symptoms seems to have been sudden and severe.

Comby [16] says of his case that the child was born at term and well formed. It was noted soon that the superior or inferior limbs, sometimes all the limbs, even the head, could not be moved freely.

It is doubtful whether these two cases can be accepted as demonstrating an acute onset of amyotonia, and the possibility of such an onset depends alone on the report of the case of Collier and Wilson.

We can hardly accept the case of Armand-Delille and Albert Weil [1] as one of myopathy, even though it was so regarded by them and by Raymond. The rapidity of development and the recovery make the diagnosis very questionable.

The acutely developing cases of amyotonia may be confused with anterior poliomyelitis and diphtherial palsy. Collier and Wilson say so far the acute cases have followed only acute bronchial disease. As a rule poliomyelitis may be distinguished, according to these writers, by the strict symmetry of amyotonia upon the two sides, the absence of local muscular atrophy, the absence of complete paralysis, and the absence of the rapid narrowing down of the extent of the regions affected which follows an attack of infantile paralysis. Granting that these points will enable poliomyelitis to be distinguished from amyotonia,

there are cases of poliomyelitis in which there is symmetrical or nearly symmetrical and general implication of the lower limbs or of all four limbs, the wasting is general in the affected parts, the paralysis is complete in the affected muscles, and partial recovery is slight or absent. It is true that such cases are the exception, and that usually poliomyelitis can readily be distinguished from amyotonia congenita.

Diphtherial palsy may cause even more confusion should acute cases of amyotonia become more common. Collier and Wilson state that diphtherial palsy is very rare during the first year of life, when amyotonia usually develops. The absence of deep reflexes and the flaccidity may be in both, but the presence of nasal regurgitation and of cardiac debility, and the history and cause of the diphtherial palsy should render impossible the making of any mistake between the two diseases in the opinion of Collier and Wilson.

We can hardly dispute, however, that diphtherial palsy may occur with so little pharyngeal involvement that it may be overlooked, and nasal regurgitation and cardiac debility may not be conspicuous in all cases of diphtherial palsy. Again, it is to be remembered that the attempt is to be made to distinguish diphtherial palsy, rare in children of the first year, from an even rarer affection, acutely developing amyotonia.

Diphtherial palsy becomes especially important in connexion with Bernhardt's [9] views regarding amyotonia. He believes a multiple neuritis or an arrest in the development of the nerves is more likely to be the cause of amyotonia than an arrest in the development of the muscles. The improvement which occurs in this disease can be explained better on nerve disturbance than on muscle disturbance. He acknowledges that disease of, or deficient development of, the nerves in amyotonia has not been determined. He has shown that multiple neuritis may occur in the first years of life, and the cases he reports bear a striking resemblance to amyotonia. Slow contraction of the affected muscles in amyotonia by direct galvanic current, he says, was observed once by Oppenheim and in one of his own cases. We must therefore acknowledge that multiple neuritis developing in the first year of life, at least as early as the fourth month, may cause a clinical picture apparently indistinguishable from amyotonia, and the neuritis is not necessarily from diphtheria. In one of Bernhardt's two cases recovery strengthened the diagnosis of neuritis, as recovery would be less likely to occur in a disturbance of the muscles than in one of the nerves.

A case which I had the opportunity to study in Dr. Griffith's wards presented the appearance of an acutely developing muscular dystrophy, and is similar to the case reported by Armand-Delille and Weil. The complete recovery after some weeks suggests multiple neuritis, and yet pain was never a prominent symptom, and objective disturbance of sensation never occurred.

J. G. (figs. 4 and 5) was admitted to the University Hospital on March 19, 1912. His age was seven years. Two brothers and one sister were living and well, and no children had died in the family. The patient had not used alcohol, and alcoholic neuritis is very rare in children. He had had no symptoms of diphtheria. His teacher had noticed that he had been very dull mentally for two months. He had masturbated. He went to school until about six weeks before he came to the hospital, and he was then noticed to be walking slowly. He was said to have fallen on the steps three weeks before admission, and following this had pain in both lower limbs and the right upper limb. It was difficult to judge concerning the character of this pain. It did not appear to have been severe, and he had none when he came under the observation of physicians. It may have been from bruising of the muscles in the fall, or it may have been from use of weak muscles, and it is even possible that the statement concerning pain was incorrect. The weakness antedated the fall.

I found the pupils equal, and the irides reacting normally to light and in accommodation. The limbs were rather massive, suggesting the possibility of pseudo-hypertrophy. When he was placed at full length on the floor and told to raise himself, he turned over on the knees and palms of the hands, placed the right hand on the right thigh, but was unable to take the left hand from the floor and to raise the body above this position. When he was allowed to sit on the floor the muscles of the back at times were too weak to support him, and he fell backward and struck the head in the occipital region with great force. When he was lying in bed he could lift the lower limbs with difficulty, and could move them at all parts, but could not move them against slight resistance. The upper limbs were as weak as the lower, notwithstanding the apparently good muscular development. A brother of the patient, a little older, examined by me, was normal physically and mentally.

Extreme hypotonia certainly is not a common condition in myopathy, but Batten believes that marked flaccidity is present in many cases. I have never seen myopathy with the extreme hypotonicity of amyotonia, such as was present in my case of amyotonia, when the thighs

FIG. 4.—J. G. Excellent muscular development, but great weakness of rapid onset with recovery.

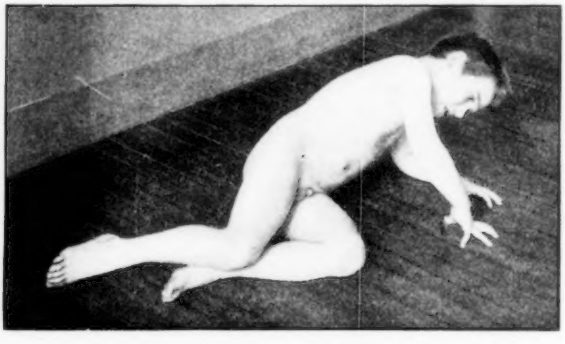


FIG. 5.—J. G. Showing attempt to climb on the lower limbs, as in pseudo-hypertrophic muscular paralysis. The photograph shows almost the full power of the boy. He was able to turn over a little farther than is represented, and to place the right hand on the right thigh.

could be placed close against the trunk and the heels behind the occiput; nor so intense as described by Collier and Wilson when they say that in several cases, including one of their own, the position which the foot assumed at rest was with the whole length of the dorsum of the foot lying along the front of the tibia. They state that the wrist and fingers can often be over-extended so as to come into complete contact with the back of the forearm.

Localized wasting is not always present in myopathy, and the atrophy may be general; still, localized wasting is a common feature of the early stage of myopathy, and its occurrence in amyotonia has not been observed. General wasting may occur in amyotonia, as in Thorspecken's case [57]. This case was typical in the absence of family disease, in the hypotonia, and of electrical reaction and in improvement. Atypical were general localization and symmetry of the paresis, the condition of the reflexes, muscular atrophy, the great atrophy of bone, and impairment of sensation, but this last-mentioned symptom seems doubtful. Cassirer says muscular atrophy does not belong to amyotonia, but Thorspecken finds smallness of muscles mentioned by many writers, and he thinks it is a fairly regular finding, and is masked by overgrowth of fatty tissue. The bone atrophy was found by the X-rays, and this method of examination has not been employed in other cases.

The untrustworthiness of progressive improvement in amyotonia as distinguishing it from myopathy is emphasized by Batten. As he says, in not a single case of amyotonia has recovery occurred; as the child develops, a certain gain of power has taken place, so that he may learn to stand or walk in a fashion. In Batten's case, D. S., improvement was said to be marked, but the boy could not stand alone, although he could do so with a little support. In many cases of amyotonia the condition has been progressive deterioration, not amelioration. In the case of amyotonia reported by Griffith and Spiller improvement for a time was marked, and this is remarkable in consideration of the pronounced and progressive changes of the nervous system, but, as in many other cases, the improvement was not permanent.

It is not because the period of observation in cases of amyotonia has been short that improvement is not great. In the case reported by Carey Coombs [17] the improvement after ten years was slight. The child was ten years old, and the condition had been present since birth. The upper limbs were more affected than the lower, and the hands were more affected than the rest of the upper limbs, so that there was localization in this case. In the study of any new disease experience teaches

that certain statements may need modification, and that features considered sharply defined are of less importance than they at first seemed. Thus Collier and Wilson, writing in BRAIN (vol. xxxi, 1908), stated regarding amyotonia: "In no case has the least tendency to exacerbation of the disease been observed." In the next volume of BRAIN (vol. xxxii, 1909), these same authors, in reporting two cases, remark: "This is one of the only two cases that have come under our observation in which progressive deterioration has occurred." From the pathological point of view improvement appeared unlikely; they could detect no evidence of regeneration or of reparatory changes in the muscles.

On the other hand, myopathy may be arrested for a long period of years, or there may be improvement, usually temporary, and possibly obtained by enabling the patient to use the less affected muscles to better advantage, or by strengthening these muscles, or in rare instances recovery may ensue. Erb said he had seen only one case of recovery in myopathy. Marina's case he regards as not fully established as regards diagnosis. Erb's case [24] was a typical one of the juvenile type, and the patient was "practically cured" (as he expresses it) after six years, although some trifling defects remained.

Jendrassik [38] accepts Marina's case as one of myopathy, but he does not accept the case of Armand-Delille and Weil. He states that in Marina's case and also in Erb's the weakness was not great. He reports two cases of dystrophy with almost complete recovery. He says in all the cases the improvement occurred at the period of greatest physical development, i.e., at puberty; in Erb's, Marina's, and his own two cases the improvement occurred when usually rapid physical development takes place.

Gordon Holmes [36] reported a case of arrested myopathy. A man, aged 60, was found to have extreme weakness of the orbicularis palpebrarum of each side, slight weakness of the orbicularis oris, and the cheeks were remarkably flat and thin. Since he was 10 years of age he had not been able to whistle properly. The muscles which depress the arms were weak, and there was considerable wasting of the lower part of each pectoralis major, and atrophy of the upper portions of the trapezii. The man was unaware of the muscular abnormalities. His daughter and nephews had typical myopathy. Holmes regarded the case as one of myopathy which appeared early, but ceased to develop at a certain stage of its evolution.

Batten stated that in many cases of dystrophy it was admitted that

there was evidence that the patients had had weakness of the face at birth, and when seen between the ages of 30 and 40 they still had the weakness of the face muscles, but no evidence of any progress of the disease.

Stanley Barnes has seen two cases of the Landouzy-Dejerine type; the patients were over 50, and in each there was no reasonable doubt that the pectoralis major had been absent for twenty-five years, and that the myopathy had not progressed for many years.

The only case of what seemed to be myopathy in which so great improvement occurred that it amounted to recovery which has come under my observation is the following: A man, aged 24, consulted me on October 27, 1904. None of his brothers or sisters had a similar disorder, although he had five brothers older than himself. He may have had typhoid in 1902, but it is not certain. When I saw him he had been complaining of weakness in the right lower limb about a year and a half. The muscles of the anterior part of the left thigh had seemed weak to him, but the weakness was not pronounced. During the three weeks before consulting me he had had moderate pain in the anterior muscles of the right thigh, probably from over-use of weak muscles, as he never had it before this time or later. He had lost about 25 lb. within the previous two years. He had much difficulty in walking, and could walk only a square or two.

On examination, the thighs were equally well developed, and measured about 16 in. in circumference in the middle. The right calf was large, and much larger than the left, which appeared atrophied. The circumference of the middle of the right leg was 13½ in.; of the left leg, 12¼ in. The left calf was soft and flabby; the right calf was very firm. He could not stand on the right foot alone as he could on the left foot.

Flexion of the right thigh on the abdomen was somewhat impaired, and flexion of the right leg on the thigh and pushing with the right foot against the hand were a little impaired. The patellar reflex was present on each side, but was not very prompt. The Achillis reflex was hardly perceptible on the left side, and was lost on the right side. Sensation was not affected in any part of the body. The trunk, upper limbs, and face were not affected. Faradic contractility was prompt in the muscles of the left calf, but was lost in those of the right calf. Galvanic reactions were not taken. He was given massage.

This patient was last seen by me on June 13, 1912. The extraordinary firmness of the right calf had almost disappeared, and only a small mass

of unusually firm tissue, about the size of an English walnut, remained. All weakness had disappeared, and he could walk fifteen miles daily with ease. The Achillis reflex was still lost on the right side. The patellar reflexes were nearly normal, possibly a little diminished. The peroneal supply on each side was unaffected.

The interesting features of this case were: weakness of the right lower limb, chiefly in the thigh, developing gradually during a period of one and a half years; possibly some weakness of the left thigh; apparently pronounced pseudo-hypertrophy of the right calf; atrophy of the left calf; diminished patellar reflexes; loss of Achillis reflex on the right side, and almost loss on the left side; absence of all objective and subjective sensory disturbances, except moderate pain in the right thigh in the weakened muscles of only three weeks' duration and probably from over-use; recovery during a period of almost eight years under massage and systematic exercise. The diagnosis of myopathy in this case would hardly have been disputed if recovery had not occurred. It is possible that typhoid fever may have been the cause of the weakness, and yet there was only an uncertain history of a disease that might have been typhoid; this had occurred two years before I saw him, and about six months before the onset of the weakness. The affection of both lower limbs made the diagnosis of thrombosis improbable. Hard patches in muscles are not uncommon in myopathy.

Typhoid fever may be a cause of myopathy, as Guillain has shown. He remarks that a few cases in literature have demonstrated the existence of true muscular hypertrophy as a result of typhoid. He gives the published cases to 1907 (Friedländer, Lesage, Cerné, Babinski). This enlargement of muscles appears to be a true muscular hypertrophy, with increased motor power, with diminution of faradic and galvanic contraction, without reaction of degeneration, and with exaggeration of tendon reflexes in certain cases, but not in all, and with limitation to one limb or part of one limb. The cause appears to be vascular lesions, especially phlebitis, and the condition an angio-myopathy.

Guillain distinguishes this hypertrophy from the functional or physiological muscular hypertrophy, the muscular hypertrophy of congenital myotonia, the muscular hypertrophy often associated with athetosis, the prodromic muscular hypertrophy of progressive atrophic myopathy, and the muscular hypertrophy of the hyperplastic muscular dystrophy of Talma.

In addition to this form of myopathy Guillain describes another form following typhoid fever, of progressive development and implicating

many muscles, and he refers only to three cases: one of Friedländer, one of Josserand, and one of his own. The diagnosis of myopathy was confirmed by necropsy in Friedländer's case.

Guillain [32] believes he has observed many cases which demonstrate that myopathy may be acquired, and possibly from infection or intoxication. This is interesting in view of the cases of amyotonia developing acutely after pulmonary disease.

FIG. 6.—Myopathy with improvement. Atrophy of shoulder-girdle and upper part of upper limbs, "winged scapulæ."

I have known distinct improvement to occur in an advanced case of myopathy. E. S. (fig. 6) came to the dispensary of the University Hospital, on July 10, 1911. He was aged 19. A year previously he fell from a scaffold, a distance of sixty feet, and possibly struck on his shoulders. He was able to resume his work the same day, but the

following day his arms were stiff and painful, and remained so for two days. From that time he could not lift anything heavy, and could do only light work. He noticed about four months later that the muscles of both shoulders were wasting, and that he had difficulty in using them. Since that time until the present the muscles have wasted, and he can raise the upper limbs to the level of the shoulders only. The deltoid, biceps, triceps, and pectoral muscles are much atrophied. No fibrillary tremors are observed. There are no sensory disturbances for touch and pain. There is no spasticity. The patellar reflexes are present, but not increased. There is no family history of similar trouble. A positive Wassermann reaction was obtained by Dr. Corson-White. Two brothers who were examined were normal.

I saw this man again in March, 1912. He was then under the care of Dr. John K. Mitchell. The atrophy conformed to Erb's juvenile type, and apparently had been started by the trauma, which is an interesting fact. No symptoms in the lower limbs suggested a cervical spinal lesion. Dr. Mitchell had ordered massage, and decided improvement had been obtained. There was distinct increase of power in the arms, hands, and legs. The man was able to comb his hair with his right hand, and this he had not been able to do before the treatment. He had found that the circumference of the upper limbs just above the elbows was 1 in. greater than it had been. He could raise the hands, when clenched, above the head. There probably has been no permanent arrest in the muscular atrophy, but important is the decided improvement in a case of myopathy, showing that improvement is not a feature of great value in the differential diagnosis between myopathy and amyotonia.

The failure of return of deep reflexes is common to both myopathy and amyotonia, and although return has been observed in the latter and not in the former, it is questionable whether great importance can be placed on this fact.

Failure of extension of the disorder from muscle to muscle in amyotonia at the present time appears as an important diagnostic sign, and yet who can tell how soon some one may report a case of amyotonia, with gradual spreading of the condition.

On the one side we have Batten urging the classification of amyotonia under myopathy, and on the other, Collier and Wilson and many others opposing this classification. Collier and Wilson remark that the similarity of the morbid anatomy of amyotonia to that of the myopathies is certain and does not admit of any discussion, but the

clinical aspect of this disease is so widely different from that of any hitherto described form of myopathy as to warrant the retention of a separate name for what they call a distinct clinical entity. I have attempted to show in this paper that many of the so-called distinguishing features of amyotonia belong also to myopathy, but after all we must acknowledge that amyotonia has distinguishing features, observed in by far the greater number of cases, and that the cases with exceptions do little more than show that there may be a transition from amyotonia to myopathy, without proving that the two diseases are identical, any more than transitional cases between myelopathy and myopathy prove identity of disease.

There are a few cases of amyotonia which are typical clinically, and in which the lesions were confined to the muscular system; in order of publication these are the cases of Spiller, Lereboullet and Baudouin, and Councilman and Dunn. Possibly the case of Finkelnburg may be included. The pathology in these cases may be arrest in the development of the muscles with or without added muscular atrophy. Thorspecken [57] believes that not a single reported case of amyotonia can be regarded as one of arrested development, except possibly that of Archangelsky and Abrikosoff. In this case general and pronounced muscular atrophy of bone and contractures showed much resemblance to myopathy. Increase of connective tissue nuclei and of interstitial fat tissue are more in favour of disease changes in fully developed elements, but in my opinion do not exclude the possibility of arrest in development, at least as a part of the process. One may readily believe that tissue arrested in development would be more liable to degeneration.

In my case [53] increase of connective tissue nuclei and of interstitial fat tissue was relatively slight, and Councilman and Dunn in the report of their case show how difficult it is to judge of the intensity and importance of such findings. My case was a typical one of amyotonia, and although objection has been made to it by a few writers, it is very evident that some of these writers have never read my papers. It is impossible, for example, to reply to a statement that a case "nicht über allen Zweifel erhoben ist," or "nicht ganz typisch ist," but when Gött and Schmidt state that the child I described was idiotic and had strabismus and amaurosis, I can only reply that they know more about the patient than I do. There is no remark in my papers that suggests idiocy in this child, and I have shown by a statement from Professor de Schweinitz of the Ophthalmological Department of the University of Pennsylvania that the ordinary concomitant squint present in the case

was not the strabismus from ocular palsy, and that it is very doubtful whether the child was blind. This case was carefully studied clinically and by microscopical specimens, and microscopical sections were made from various levels of the spinal cord, from muscles from the sole of the foot, calf, back of the trunk, and arm, and from peripheral nerves.

The case of Lereboullet and Baudouin cannot be rejected merely because convulsions occurred, and that during these convulsions the muscular atony disappeared. The patellar and olecranon reflexes were diminished, but not lost. The exaggeration of reflexes later in the course of the disease is not sufficient to exclude amyotonia, and it was probably the result of the convulsions. A child with amyotonia is not exempt from convulsions.

The findings in the case reported by Councilman and Dunn [19] were purely muscular. The amount of connective tissue was increased. Some fibres appeared like normal adult muscle-fibres, others were very small, and under low power appeared as accumulations of cells arranged in fasciculi. The nuclei in the small muscle masses seemed to be extremely numerous. The apparently great number of nuclei was due to the number of the fibres, and when a single fibre was followed along the nuclei were not more closely set than they were in the large fibres. Occasionally fibres were seen which were hollow, with fibrillæ at the periphery, presenting much the appearance of embryonic fibres. There was no general fatty degeneration of the muscles, but in certain muscle-fibres there was a large amount of fat. The connective tissue in the muscles was relatively increased, but it was uncertain whether there was an actual increase in this tissue. The spinal cord was practically normal.

There are other cases of amyotonia with pronounced muscular changes and comparatively slight alteration of the nervous system, such as those of Baudouin, and Archangelsky and Abrikosoff. It is well to remember that while myopathy usually is without marked alteration of the nerve-cells of the anterior horns, even when the disease has existed so long as in the case reported by Duchenne [22] in 1872, by Landouzy and Dejerine [40] in 1886, and by myself [54] with the pathological findings in 1900, still there are transitional forms in which moderate changes of the anterior horn-cells are detected.

The subject of degenerative changes occurring in the lower motor neurones in muscular dystrophy has been discussed by Gordon Holmes. [35]. He reports a case of this disease in which there was considerable diminution in number and size of the nerve-cells of the anterior horns

and atrophy and diminution of fibres in the ventral roots. He refers to a number of similar cases in literature. He thinks that in his case and in the majority of the others there can be no doubt that the condition was acquired, and was not a developmental defect. The nature of the cell-changes, the slight secondary gliosis of the ventral horns, the definite evidence of loss of fibres in the ventral roots and peripheral nerves, and the increase of connective tissue in the nerves, make this certain. He rejects the theory of nervous origin for the muscular atrophy in these cases, because the histological changes in the ventral horns in his case appeared to be distinct from the degenerative cell-changes he has found in any of the many spinal amyotrophies he has examined, and the muscular affection exceeded them both in degree and extent. He believes the neural changes are secondary to the primary muscular disease. He does not know of any evidence of neural degeneration secondary to disease entirely limited to muscle tissue, but he thinks it is probable that when muscle fibres undergo complete atrophy and disappear, the functional, and probably secondary thereto the nutritional, equilibrium of the neurones which terminate in these fibres must be disturbed. The terminal branches of the axis cylinders left naked by the disappearance of the muscle-fibres probably will be injured and possibly destroyed by the connective tissue which proliferates secondary to the muscle disease. He refers to Baudouin's case of amyotonia congenita, and shows how closely it resembles the case he reported. Baudouin himself spoke of the muscular changes, "telles qu'on peut les voir dans les myopathies." Holmes says that the morbid anatomy of Baudouin's case was identical with that of a considerable number of undoubted cases of muscular dystrophy. He states that the origin in his case and Baudouin's must have been similar, as Baudouin believed the abnormal condition of the muscles could not be regarded as merely an arrest of development, and must have been an acquired condition. Owing to its intensity the muscular alteration of Baudouin's case could scarcely have been secondary to the simple atrophy of the ventral horn-cells, and its nature, too, was distinct from that of the neuropathic atrophies. It must be concluded, Holmes thinks, that the disease of the muscles was an acquired regressive affection, dependent probably on an intrinsic developmental anomaly. From the pathological and clinical points of view Holmes thinks Baudouin's case differs from one of myopathy only in the commencement during intra-uterine life. The clinical manifestations so closely resembled those of myopathy that it seems unnecessary to place the case in a separate

class. The most important distinction of amyotonia is that it is not progressive, and that amelioration may occur. Even if amyotonia were congenital myopathy, these distinctions would not be surprising in view of the difference of the nutritional conditions of the individual before and after birth, and the changes in the mutual relationship of the muscular and nervous systems in intra- and extra- uterine life.

It seems probable to me that an arrest with later atrophy may occur in the peripheral neurones as well as in the muscles in some cases of myopathy. It is common to find more than one defect in development. Oppenheim has emphasized this as regards myasthenia. Cataract with muscular atrophy is another example. The case of myopathy of long standing referred to above shows that great destruction of muscle does not lead necessarily to degeneration of the peripheral neurones.

Archangelsky and Abrikosoff regarded the changes in the cord in their case partly as arrest in development of the grey substance, and partly as a retrograde change. Most muscle-fibres were thin, but their structure was preserved; there was no nuclear proliferation of the muscle-fibres nor overgrowth in the connective tissue, therefore they regarded the muscular condition as arrested development. These findings in the muscles resemble those in the cases of Spiller, Finkelnburg, Lereboullet and Baudouin, and Councilman and Dunn, but Archangelsky and Abrikosoff found diminution in size of the anterior horn-cells, and this finding is like that in the case of Baudouin.

It seems, therefore, that the symptom-complex of amyotonia may depend on purely muscular lesions (Spiller, Lereboullet and Baudouin, Councilman and Dunn), or these muscular lesions may be associated with alteration of the cells of the anterior horns, which in some instances seems to be slight (Lereboullet and Baudouin, Archangelsky and Abrikosoff), in others intense, and when this cellular alteration is intense the distinction from the Werdnig-Hoffman type of atrophy may be difficult.

The Relation of Amyotonia to the Werdnig-Hoffmann Type of Atrophy.

Rothmann [47] has considered this aspect of the subject. Heredity, progression of the disease, reaction of degeneration, and commencement in the proximal parts of the limbs are the most distinguishing features of the Werdnig-Hoffman type. This form has occurred without familial character, as in the cases of Thomson and Bruce, Bruns, Wimmer, Armand-Delille and Boudet. In amyotonia Rothmann believes the

spinal process has reached its height at birth, and improvement depends on the condition of the persisting anterior horn-cells. The Werdnig-Hoffmann atrophy, beginning in the second half of the first year or later, has a more gradual destruction of the nerve-cells, and yet Rothmann acknowledges that amyotonia beginning in the first months of life may show much improvement. The improvement in one case, the progression to death in the other are not sufficient to distinguish the two processes. The progression to death may be greatly delayed, as shown in three of Bruns's cases. Rothmann does not regard the reaction of degeneration as an important distinction, and this subject will be considered a little further on in this paper. As for the pathological findings Rothmann thinks they show gradations.

Rothmann's conclusions are:—

Amyotonia in the majority of cases anatomically is a disorder of the anterior horn-cells, and these cells may completely disappear.

All gradations exist between amyotonia and the Werdnig-Hoffmann type, so that sharp distinctions cannot be made between these diseases.

Transitional forms occur between the spinal muscular atrophy of fœtal origin (amyotonia) with affection of the lower cranial nerve-nuclei, and the nuclear loss of Möbius ("Kernschwund") with implication of the spinal cord.

Cassirer [12] regards as important distinctions that amyotonia is not progressive, and the Werdnig-Hoffmann atrophy first is seen in children in the second half of the first year of life. It is questionable whether these can be regarded as important. It is difficult to say exactly when a disease begins, especially when the date of its commencement is often determined by a more or less ignorant parent, and Wimmer's case [58], which he regarded as belonging to the Werdnig-Hoffmann type, was congenital. Cassirer is not willing to class amyotonia under spinal affections, and in his opinion it is closer to myopathy.

The cases of amyotonia with intense alteration of the cells of the anterior horns seem to indicate that the disease may be without amelioration, and even may be progressive. Such cellular changes are usually progressive in spite of all we do to check them.

Batten [4] acknowledges the difficulty in distinguishing between amyotonia congenita and the Werdnig-Hoffmann paralysis. His points of distinction are that in amyotonia a child as a rule can perform all movements in a feeble manner, and there is not the marked degree of flaccid paralysis seen in the case of spinal atrophy. Although hypotonia is present in cases of spinal atrophy, it is not so marked

as in cases of amyotonia. The intercostal muscles are commonly paralysed in the spinal atrophy of infants, whereas in amyotonia they are less affected. In brief, in spinal atrophy the paralysis is more marked and the hypotonia less marked than in cases of amyotonia.

It is indeed a question whether further experience will justify these distinctions. They depend upon degree rather than upon quality of characteristics, and do not apply to some of the cases of amyotonia described with intense pathological change of the anterior horn-cells. In a mild case, one in which the spinal changes have not advanced far, and especially one in which the lesions are purely or largely muscular, all movements may be possible.

The flaccidity has been very great in a number of cases of amyotonia, and loss of power has amounted to complete paralysis (Archangelsky and Abrikosoff). In some of the cases of the Werdnig-Hoffmann type the flaccidity has been pronounced, and was so in a case reported recently by Batten and Holmes [8]. These authors had made a diagnosis of the Werdnig-Hoffmann type, but some who had seen the patient had regarded the disease as amyotonia. It is difficult to understand how the intercostal muscles could be little affected when the changes in the anterior horn-cells of some of the cases of amyotonia are so great. One is reminded by these distinctions of the attempt to separate chronic poliomyelitis from progressive spinal muscular atrophy.

The intercostal muscles have been reported as affected in a number of cases of amyotonia. Lugenbühl [42] remarked that the muscles of the thorax and neck were badly developed, and were not active. Pollak [46] said of his case that the thorax and back muscles were paralysed.

In the case reported by Griffith and Spiller [31] there was no history of acute disease. The mother said the boy had never been able to move his legs effectually or to handle objects. He took slight notice of anything, and had never been able to sit up. The legs were motionless and flaccid, the feet in position of foot-drop. The muscles of the legs were soft, but without actual atrophy. The toes and legs could be moved freely by the child when he was stuck with a pin. Passive movement at the knee-joint was unusually free, but there was contracture at the ankle. The muscles of the arms were soft, but not atrophied. The child was able to move the arms very feebly and slowly, and with little ability to handle objects. No tendon reflexes were obtainable. He was unable to sit unsupported, and when held in a sitting position extreme kyphosis developed, and the head dropped in any direction in which gravity acted upon it. When released the trunk would fall in a similar manner, some-

times forward, with the head against the ankles and the arms lying helplessly where they happened to be, and the child was unable to change this position.

Two and a half months after the first observation the intellectual power was found improved, the child took more notice of objects, the power in the upper limbs had increased, and he could now grasp a biscuit and eat it unaided. All movements of the upper limbs were still slow and feeble. There was slight increase of movement in the lower limbs. Under electrical or other stimulation there was decided increase of movement in the limbs, but no distinct muscular contraction was obtained by electricity, faradic or galvanic.

The findings in this case were very similar to those of Rothmann and those seen in the Werdnig-Hoffmann atrophy. I should like to refer to the fact that this child, as in the previous case reported by myself, took little notice of objects, as in no way indicative of poor sight. A child so weak has little interest in what is going on about him.

In the case reported by Gött and Schmidt [27] the clinical picture resembled amyotonia more than the Werdnig-Hoffmann type, except in certain features, viz., the absence of improvement, with a tendency to increase in the symptoms, the presence of reaction of degeneration (this is said to be always absent in amyotonia, but in Thorspecken's case slow reaction was obtained), and the presence of fibrillary tremors (these have never been seen in amyotonia, and are regarded as rare in the Werdnig-Hoffmann atrophy). Opposed to the Werdnig-Hoffmann type were the absence of heredity and familial tendency, and the appearance of symptoms immediately after birth, and not in the course of the second year of life. The findings were those of the Werdnig-Hoffmann type. Gött and Schmidt try to answer those who regard amyotonia and the Werdnig-Hoffmann atrophy as the same disease, but the very case they report is in support of a close relationship between the two. The cases of Wimmer, and Gött and Schmidt show that a congenital form of spinal muscular atrophy exists. The latter case is important, for it had the symptoms of amyotonia, including the hypotonia, and other signs showing clinically implication of the spinal cord. The muscles were much degenerated, the nerve-cells of the anterior horns much diminished in number and size, and the anterior lumbar roots were not so well medullated as the posterior.

Marburg [43] also declines to accept amyotonia as identical with the Werdnig-Hoffmann atrophy. He lays much stress on the absence of the fatty pigmentary degeneration of the nerve-cells in the Werdnig-

Hoffmann atrophy, which is so common in the Aran-Duchenne type, and has never been seen in very early childhood. Since his paper was written, Zatelli [60] has reported the finding of distinct fatty pigmentary degeneration of these nerve-cells, recognized by the Marchi stain, in a case of the Werdnig-Hoffmann atrophy. This seems to be the only case in which this change of nerve-cells has been found in children.

The distinctions Marburg makes are:—

Amyotonia.	*Werdnig-Hoffmann Atrophy.*
Congenital.	Acquired early.
Usually single case.	Usually familial.
General hypotonia.	Localized atrophy, beginning in pelvic girdle.
Atrophy concealed.	Atrophy easily recognizable.
Loss of tendon reflexes.	Tendon reflex activity in proportion to the atrophy.
Electrical irritability (?) or amyotonic reaction (faradic lost, galvanic normal).	Reaction of degeneration.
Improvement.	Progression with constant impairment.

These features, Marburg holds, are the most important, and show the differences between the two diseases. The congenital origin, it has been shown, is not always present in amyotonia, and Wimmer's case of the Werdnig-Hoffmann type and the case of uncertain classification of Gött and Schmidt were congenital. Familial cases are infrequent, but probably occur in amyotonia, and many cases of the Werdnig-Hoffmann type have not been familial. Hypotonia may be pronounced in either affection, although it is likely to be more intense in amyotonia. The atrophy in amyotonia may be distinct, and may implicate the bones, as in the case of Thorspecken. The condition of the tendon reflexes as a point of distinction is unreliable, especially in such young children. Galvanic and faradic reactions were lost in the case of Griffith and Spiller. In Rothmann's case strong faradic irritation gave only slight contraction of the flexors of the forearm, galvanic gave slow contraction, but KClC was greater than the AnClC. This case was studied in Oppenheim's clinic while the child was living, and was accepted as one of amyotonia.

As regards electrical irritability, Cassirer states that the determination of the electrical reactions in amyotonia is difficult in so young children. Some investigators have found that the children endure strong currents easily, but this Cassirer and some others dispute. In no case has a

very exact electrical examination been made; according to Cassirer, in general it may be said there is diminution of the irritability, but no qualitative change. A peculiar reaction has been described by Collier and Wilson, and this they call the amyotonic reaction; the muscles react much below normal to a strong faradic current, whereas to the galvanic current the formula and form of contractions are normal. Cassirer says his experience shows that this difference in reaction to the two currents is not present in all cases.

All the muscles and nerves reacted to the faradic and galvanic currents in Thorspecken's case, but to stronger currents and in narcosis. Without narcosis the reactions were uncertain in some of the muscles. Slow reaction to the galvanic current was obtained in two muscles. Oppenheim is said to have had a similar finding in one case of amyotonia.

Improvement is not confined to amyotonia, and in many cases of this disease has not been pronounced, as has already been stated.

It would seem, therefore, that the distinctions given by Marburg are not so positive as they appear at first sight. He regards amyotonia as fœtal acute poliomyelitis, but he acknowledges that the existence of fœtal poliomyelitis has not been positively demonstrated. I do not know of any other writer who has accepted this view. I have seen nothing in the two cases I have studied that would justify such an opinion, and it is disputed by Thorspecken, who distinguishes amyotonia by the great extent and symmetry of the muscular disorder, by the absence of complete loss of function in a single muscle, by the characteristic electrical reaction (of somewhat questionable value), by the absence of vasomotor and trophic disturbances, and by improvement after a period of years.

Batten has attempted to demonstrate that intra-uterine poliomyelitis may exist. The first case reported by him in his paper does not afford absolute proof of fœtal poliomyelitis, but makes it probable. Especially characteristic of poliomyelitis is the elongated patch with almost complete disappearance of medullated fibres in the right ventral horn of the sacral region, represented in fig. 4 of Batten's paper. A patch of this character in the ventral horn, consisting of neuroglia, and without medullated nerve-fibres or nerve-cells, is very suggestive of poliomyelitis. Marburg's view that amyotonia is fœtal poliomyelitis receives some support from Batten's case [5], but in none of the cases of amyotonia have findings exactly like these been described, in none were these characteristic patches of neuroglia tissue representing scar formation following an inflammatory exudate.

The Distal Type of Myopathy.

Cases of the distal type of myopathy have been reported by Oppenheim and Cassirer [45], Gowers [28], Dejerine and Thomas [21], Spiller [55], Batten [6], and Cottin and Naville [18]. Campbell's case [10] is somewhat doubtful. To this list I now add another case, although it is without necropsy.

The case of myopathy of the Aran-Duchenne type (the atrophy began in the hands), reported by Merklen and Schaeffer [44] was purely clinical. Reaction of degeneration was present in some muscles of the lower limbs.

In my paper in which a case of the distal type of myopathy was reported, I emphasized the importance of recognizing as belonging to the peroneal (Charcot-Marie-Tooth) type the long-continued and sharp limitation of the atrophy to the parts below the knees and elbows. Cases in which the thighs and upper arms are wasted may belong to this type but they are not questionable.

Batten thinks the disturbance of peripheral sensation, often found in the peroneal type, points strongly in favour of the peroneal type as distinguishing it from the distal type of myopathy, and implication of facial muscles is a point strongly in favour of the muscular origin of the disease.

Hoffmann, however, accepts involvement of the facial muscles as a part of the peroneal type, as Batten mentions, and in Oppenheim and Cassirer's case of myopathy implication of the cranial nerve-supply was slight. In myopathy the atrophy may begin in the distal parts of the limbs, but sooner or later extends beyond them, and the trunkal muscles are likely to be affected. Sensory disturbances are so often absent in the peroneal type that in many cases the condition of sensation affords no means of differential diagnosis.

Cottin and Naville believe that in peripheral myopathy, as regards the hand supply, the atrophy has not the same distribution in the beginning of the disease as in the Aran-Duchenne atrophy. In the peripheral myopathy the hands fall and the fingers are flexed, and atrophy appears later, whereas atrophy is always early in the Aran-Duchenne form, and does not effect the extensors of the thumb and fingers until late. Peripheral myopathy, like the juvenile form, affects especially the extensors. These authors believe that peripheral myopathy begins late (middle life), is not hereditary nor familial, and is more common in females. In my case it began about the age of 26 years, and was in a male. In

Gower's case it began at the age of 10 or 12 years, and was in a male. In myopathic families females are affected later than males, and less severely, or even escape. The frequency of the peripheral myopathy in women affords a contrast to the rarity in women of the Aran-Duchenne and Charcot-Marie-Tooth types of atrophy, in which the distribution and time of onset are much the same. These conclusions of Cottin and Naville are untrustworthy, because they employ three cases only, and ignore those of Gowers, Spiller, and Batten. Gowers's case is referred to as an atypical form. It would seem from the work of Cottin and Naville that in the peripheral type of myopathy the extensors of the hands and fingers and the extensors of the toes are chiefly affected. In Batten's case the patient was a boy aged 3 at the onset of the symptoms. Another case now reported by me is similar in that a young boy was affected.

The boy described by Batten was well until the age of 3, when he contracted measles. A few weeks later the mother noticed dragging of the left leg. Seven months later the right leg became affected, and power in the hands began to be lost at the age of 6. The wasting of the arms and legs progressed slowly. At the time of examination (18 years of age) there was much wasting of all the muscles below the knee and a considerable amount of wasting of the thighs. The foot was in a inverted position, and the boy walked on the outer side. There was marked wasting of all the muscles of the arms below the elbow, and but little power of movement in the hands and forearms. The upper arms and shoulders were well developed. The muscles of the face and trunk were normal. The deep reflexes of the leg were absent. There was no response to faradism or galvanism in any of the muscles below the knee or elbow. Sensation was normal. There was no marked vaso-motor disturbance in the legs. Batten, some years previously, had shown this case as one of the peroneal type following measles. At the time of the presentation of this patient he reported the occurrence of the distal type of myopathy in several members of one family. These cases called forth considerable difference of opinion. Holmes remarked that the age of onset of peroneal palsy was higher than in Batten's cases.

A recent case which I have studied is as follows: T. B. (figs. 7 and 8), white, aged 9, came to the Nervous Dispensary of the Hospital of the University of Pennsylvania on June 27, 1911. The first child was born at the sixth month, and died when a few months old. The patient also was born at the sixth month. The labour was normal. He weighed five pounds at birth, was very small, and developed slowly. When he

was 3 years old he gradually developed weakness and deformity of the ankles and legs, but there is some doubt whether the weakness began in the ankles or in the thighs; the much greater atrophy of the legs would suggest that the atrophy began in these parts. He was very healthy when 2 years old, and better developed than most children of the same age.

FIG. 7.—Distal type of myopathy. The photograph shows the bilateral foot-drop and greater wasting of the lower limbs below the knees and atrophy of hands and forearms.

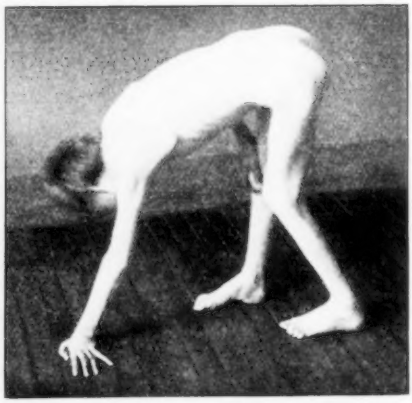


FIG. 8.—Distal type of myopathy. Photograph shows the extent to which the patient was able to rise from the floor. The method of rising is like that of pseudo-hypertrophic muscular paralysis.

In June, 1911, the head was not affected apparently. The movements of the hands were somewhat awkward and ataxic, probably from weakness, and the muscles of the right hand appeared as if they were beginning to atrophy. Both scapulæ were prominent and winged.

The muscles of the back and thorax were small, but there was no localized atrophy in these parts. The feet were placed far apart, and there was grave foot-drop on each side, and steppage gait. When rising from the floor he climbed upon his lower limbs. There was symmetrical atrophy of all the muscles below the knees. The calf muscles seemed stronger than the others. Sensation was normal for pin-prick, but the examination was not satisfactory in this respect. The patellar reflexes were absent and there was no ankle-clonus. The big toes did not move upward in testing for the Babinski reflex. The Wassermann test was negative, the Noguchi positive.

In March, 1912, the atrophy of the small muscles of the hands was pronounced, and much more so than in June, 1911. In raising himself he could not take both hands from the floor.

The boy was examined by me again on December 26, 1912. He was able to walk without support. The lower limbs were weak and the gait was distinctly steppage, because of the bilateral foot-drop. The lower limbs were greatly wasted in all parts, and he was weaker than at my last examination. The middle of each leg measured 16 cm. in circumference. He had very little movement in the ankles and none in the toes. The legs were much more wasted than the thighs. The hands were very much wasted, and equally so. The thenar eminence had disappeared, and the hand was of the simian type, with over-extension of the first phalanges of each side. He moved all the fingers freely, but weakly. The forearms were more wasted than the upper arms. The power was greater at the shoulders and elbows than at the wrists. He had no biceps or triceps reflexes. He had winged scapulæ, but not the typical loose shoulders of myopathy. He had no lordosis and no distinct weakness of the thoracic muscles in breathing. The sensation was normal in all the limbs. Galvanic reaction in the muscles of the front of the left thigh and in the right biceps was about normal, although the AnCIC was nearly equal to the CCIC, but there was not the slightest slowness in the contraction.

The boy had never whistled. He could blow out a lighted match, but he did not pucker up the lips, nor did he seem able to draw up the corners of the mouth—he simply drew the corners a little backward. He closed the eyes, but not with great force, and yet one would hesitate to say that the orbicularis oculi muscles were weak. The face did not appear to be atrophied. The masseter muscles, the tongue and soft palate were normal, and there was no fibrillary twitching of the tongue. Fibrillary twitching was not noticed anywhere.

Myotonia Atrophica.

Myotonia atrophica is a rare disease in America so far as one may judge from the scarcity of published cases. The recent critical studies of Batten and Gibb, Ascenzi, Hoffmann, and Curschmann have established its position in relation to the myopathies as a distinct form, and differing in important details from Thomsen's disease.

Batten and Gibb [7] mention that in this disease the myotonic features in many cases are very limited in distribution, and occur after the muscular wasting has been present many years. They admit that muscular atrophy may develop in typical cases of Thomsen's disease. The muscular atrophy, they find, has a distribution which is characteristic, and has been present in fifteen out of twenty-seven recorded cases. There is weakness of the face (myopathic face), atrophy of the sterno-mastoids, atrophy of the vasti muscles of the thighs and dorsoflexors of the feet. The masseter and temporal muscles are sometimes affected, as are also the extensors and flexors of the forearm. The disease tends to affect members of a family in the same generation, and is more frequent in the male sex. The distribution of the atrophy in some cases, especially in the legs, bears a resemblance to that of the distal type of myopathy. Chiefly on these considerations Batten and Gibb believe that myotonia atrophica should be regarded as a form of myopathy.

Ascenzi's reason [2] for accepting myotonia atrophica as an entity are: the great frequency of muscular atrophy and myotonia in the same person. More frequently hypertrophy is found with myotonia (athletic type), but muscular atrophy with myotonia affects symmetrical muscles, and has all the characteristics of myopathy. The atrophy probably has often escaped detection until within a few years. Hypertrophy of muscles may be associated with atrophy in the same case. The clinical picture of myotonia atrophica rests on thirty or more cases, and is fairly constant. The pathological findings are similar in myotonia and myopathy. In both males are more frequently affected, in both symmetrical muscles are involved, the proximal muscles are more affected than the distal, the visceral muscles escape, and other signs of involvement of the nervous system are wanting. Ascenzi gives a table of the reported cases. He states that the type described by Batten and Gibb is the most frequent, but irregularities in distribution of the atrophy occur in cases of this type.

The family reported by Greenfield [29] is remarkable in the

number of its members affected with myotonia atrophica and early cataract.

In the two cases reported by Kennedy and Oberndorf [39] the first corresponded to the clinical picture of Batten and Gibb. In the second case there was premature bilateral cataract.

Hoffmann [34] says that all the cases of myotonia atrophica in the literature with his own number seventy, at the most eighty. Of these five had hereditary unilateral or bilateral cataract, and three sporadic, i.e., eight altogether, or 10 per cent. Two or three cases are omitted from this list. The percentage of cases in which two so different conditions occurred is so large that a relation of cause and effect must be considered, especially as usually myotonia exists for months or years before cataract develops. If cataract were observed only in sporadic cases of myotonia, it might be supposed to be caused by the myotonia. Against this view is the fact that there are families in which some members have (1) cataract without myotonia, other members (2) myotonia without cataract, and other members (3) myotonia with cataract. The relation of cause and effect therefore can be determined, and both conditions probably depend upon a hereditary diseased anlage of the organism. The lens is from ectodermic tissue, the muscles are from mesodermic. The fact that persons with myotonia atrophica often are psychopaths is to be explained in the same way. Hoffmann says, so far as he knows, cataract has not been observed in the true Thomsen's disease, myotonia congenita without atrophy. This is true also of other forms of muscular atrophy, dystrophy, neuritis (i.e., the Charcot-Marie type), and spinal forms either acute or chronic. He refers to Lange's cases, but makes no further comment on them, and he does not refer to Hamilton's paper [33]. Lange's and Hamilton's cases make his statement as to cataract occurring only with myotonia atrophica inaccurate.

The recent review of myotonia atrophica by Curschmann [20] with a report of six cases of his own, does much to establish the type he designates by the name of Steinert as a distinct disease.

Hypertrophia Musculorum Vera.

The position of hypertrophia musculorum vera (dystrophia muscularis hyperplastica) is still a matter of dispute. Some of the reported cases have shown implication of the peripheral nerves, but the disease on the whole appears to be primarily muscular, and its place seems to be with the myopathies.

Eichhorst [23] in speaking of this type, says Auerbach believes it is only an early stage of pseudo-hypertrophy of the muscles, but against this view is the absence of proliferation of the interstitial connective tissue of the muscles, even when the condition has existed a long time. Eichhorst describes it as a rare disease, concerning the cause of which very little is known.

Talma [56] in 1893 collected the cases belonging to this type in the literature, and reported a case of his own. His patient was about 48, and had the disorder six years. Almost all the voluntary muscles were very large, and although the panniculus adiposus was well developed, the muscles stood out prominently, so that the man could have served for a model of Hercules, and yet he was weak. A piece of biceps muscle removed during life macroscopically appeared to be normal, and there was an increase of fat or connective tissue. On examination sensation was diminished.

The sarcolemmata had disappeared, the primitive bundles were not sharply defined, and they were farther apart than in normal muscles. Many nuclei were found between the primitive bundles, but it could not be determined whether these were proliferated sarcolemma nuclei or whether they had arisen in the interstitial tissue. The transverse striation had in great part disappeared. Spaces containing spindle-shaped cells were found between the fibrils of the primitive bundles. The muscle appeared to be formed by new primitive bundles, and the number of them was increased. Only those which had preserved the transverse striation were supposed to be capable of normal contraction, and the number of these was small. In strict sense it was not therefore a true muscular hypertrophy, as the muscular tissue was not normal. A piece of nerve examined also was not normal.

In a similar case reported by Auerbach the muscles of only one limb were enlarged, sensory disturbances were not present, and improvement occurred after some months. A contraction of this limb was normal at first, but the power soon diminished. In pieces of muscle removed the transverse striation was normal in almost all the primitive bundles. A slight nuclear proliferation was found. Faradic irritability was diminished.

In Berger's three cases only one limb was affected—objective and subjective sensory disturbances were present, and electrical irritability was diminished. In two of these cases only enlargement of primitive bundles was found.

Friedreich described two cases of true hypertrophy of some muscles

associated with atrophy of others. In his first case the muscles of the lower limbs were hypertrophied and very hard in voluntary contraction, and their power was increased. The primitive fibres were thick, and their transverse striation in great part normal, and among these were found wax-like degenerated fibres. In his second case, in almost general atrophy, a few muscles were hypertrophied.

In Krau's case some pain occurred, but no changes were found in the nerves. Hypertrophy of muscles was associated with weakness. Pieces of muscles were excised. Most of the fibres had transverse striation, and nuclei were found within the substance of certain muscle-fibres.

Bruch's case was in a child aged 20 months at the time of death. The muscles of the trunk and limbs were thick and hard, and their power was very great. Microscopically the muscles were normal, but thick.

In Pall's case most of the muscles of the body were enlarged and weak. The primitive bundles were found to be normal in an excised piece of muscle.

A very interesting case of this excessive muscular development with weakness was observed in our service at the Hospital of the University of Pennsylvania, and was carefully studied and reported by A. H. Woods [59], together with references to the literature. In his summary Woods described the characteristics of the disease as increased bulk of the affected muscles, which feel firm when contracted; diminished power with early fatigue; hypertrophy of individual fibres, some increase in the number of the nuclei; no proliferation of fibrous or fatty tissue, and no degeneration; tendon reflexes, mechanical irritability, and electrical reactions varying from slight diminution to slight increase; no qualitative electrical change; vasomotor changes in a few cases; some dull pain or tenderness of muscles; slow course, with little change from year to year; greater frequency of the disease in males.

In the case reported by Woods, painful muscular cramps occurred, and one of these was seen. A small mass of muscle, 2 to 4 cm. in diameter, rose up, became hard, and formed a rounded tumour, which remained a moment and subsided. Even light tapping of the muscles caused prompt contraction of fibres; in the deltoid and biceps of each side this amounted to a jerk of the whole muscle. These idiomuscular contractions are remarkable, as Babinski and Jarkowski have shown, that while they are absent in myopathy (a fact known previously), they

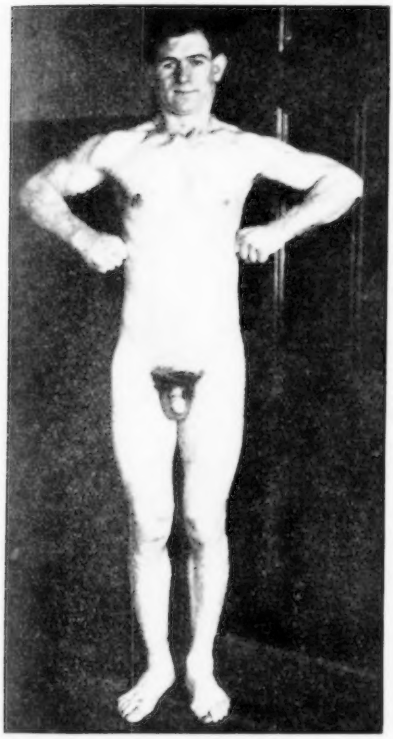
are preserved or exaggerated in neuritis and poliomyelitis. This man was examined in the university gymnasium, and although he was a day-labourer and of unusual muscular development, in muscular power he fell below a man leading a sedentary life, below even the average of 2,000 students, among whom were not merely the young and sedentary, but even some sickly individuals. He fell far below the athletic type of student, with whom he should have compared favourably; the tests being not such as require skill, but those which labourers should best execute.

A piece of muscle was excised from the left triceps and examined. It showed distinct enlargement of fibres in cross-section. The fibres were nearly round in cross-section, the diameters ranging between 70 and 180 microns; most of them falling between 130 and 160 microns; the average being 130 microns. There was no increase in fibrous tissue, endomysium and perimysium being as in normal fibres. There was no sign of fatty overgrowth, and no degeneration of muscular tissue. There was no round cell infiltration.

A typical case of this type has recently come under my observation, for which I am indebted to Dr. W. B. Cadwalader. The patient (figs. 9 and 10) is a man, aged 24. He has six brothers and three sisters, and the brothers appear to the patient to be of unusual muscular development, but without corresponding strength. I have been able to see only one of the brothers, a boy aged 12, who had an attack of poliomyelitis when 19 months old, and has an atrophied right lower limb. He does not appear to be of unusual muscular development. The patient's three sisters are said to be of normal appearance. The man is a plumber, and has done some heavy work. When he was a boy, he says, he was apparently stronger than other boys of his age, but during the past four or five years he has noticed that he is weaker than most men. Four years ago he could carry a bath-tub weighing 280 or 290 lb. upon his back, if some one placed it there, up a flight of stairs. This was difficult to do even at that time, but now it would be impossible. He states that plumbers often carry this weight. He complains of a dull heavy ache in the calves, especially in the morning when he awakens and toward evening. This pain appears to be from use of weak muscles.

When he is stripped he presents the appearance of extraordinary muscular development. His muscles stand out when contracted as do those of a very powerful man. His biceps and deltoid form large masses when the forearms are flexed upon the arms, and the latter are

drawn backward. Galvanic reaction is normal in the biceps and deltoid muscles of each side, the KaClC > AnClC, and there is no slowness of contraction. Light touch, pin-prick, moderate degrees of heat and cold are promptly felt in every part of the body. The biceps and triceps reflexes are present on each side, but not very prompt. Either



FIGS. 9 and 10.—Case of hypertrophia musculorum vera. The muscles are exceedingly well developed, and yet the weakness is very great.

forearm when strongly flexed can be extended by the examiner without much exertion, and with one hand. When either upper limb is held at a right angle with the trunk, it can be depressed by the examiner with slight exertion. There is not the slightest atrophy in any part of the body.

The lower limbs appear well developed, but they are weak. When

he attempts to run he almost invariably falls, because of giving way of the lower limbs. He can, however, stand on either lower limb separately. Comparatively little strength on the part of the examiner is required to prevent the man from raising either knee or extending either leg on the thigh. The weakness is noticed especially in climbing stairs. The patellar and Achillis tendon reflexes are about normal on each side.

The man is a Jew. I have been unable to confirm his statement that his brothers are weak, and therefore cannot be certain that the disease is a family one. There can be no doubt that the muscular development is far in excess of the muscular strength. The only sensory symptom is pain, more of a dull ache, although at times it may be more severe; this ache he has always, and has had it since boyhood. I think it is very questionable whether this could be regarded as the result of disease of sensory fibres, and attribute it to constant over-use of weak muscles.

The occurrence of muscular hypertrophy in myotonia atrophica makes the relation of muscular hypertrophy to myopathy more probable. Thus Wardrop Griffith reports a case without necropsy, but with excision of a piece of muscle which presented the symptoms of myotonia in a pronounced form, with marked atrophy of some groups of muscles and an enlargement of those of the calves. In this case there was no increase of the knee-jerks. The histological examination, he says, appears definitely to exclude pseudo-hypertrophic palsy, and to show that there was a real enlargement of the muscular fibres, and that any increase in the general mass of the muscle was not due to fatty or fibrous infiltration. Griffith [30] calls the case one of myotonia atrophica et hypertrophica. The changes in the muscles varied somewhat in the two limbs, upper and lower, but in each instance they were variations in size and in shape of the fibres, and variations in the number and distribution of the nuclei. In diseased muscles the fibres were almost circular in transverse section, and roughly speaking, twice the diameter of those in the control muscle.

A relation of myopathy in some of its types to glandular disturbance possibly may be fully established some day. It is remarkable that in a case of the juvenile type of muscular atrophy reported by J. Michell Clarke [13] there was simultaneous enlargement of the parotid glands. The submaxillary glands were slightly enlarged. This suggests the case of Schönborn, in which all the salivary glands were enlarged, and at the same time there was hypertrophy of all the muscles of the body.

Schönborn [50] thought the case was one of myopathy of toxic nature, possibly from glandular disturbance.

Sacara-Tulbure [48] reported a case of pseudo-hypertrophic paralysis beginning at the age of 48 years, in which she says a remarkable fact was the pronounced development of certain glands, as submaxillary, parotids, axillary, and inguinal. This case was with necropsy.

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Publications Recently Received.

[*Notes on a book under this heading do not preclude a subsequent review.*]

Vitalfärbung am Zentralnervensystem. Beitrag zur Physio-pathologie des Plexus Choroideus und der Hirnhäute. Von Prof. Dr. Edwin E. Goldmann. S. 60, mit 4 Tafeln. Berlin: Verlag d. K. Akad. d. Wissenschft. 1913.

This work has become of pathetic interest from the untimely death of its author. In his researches on serous membranes and their functions in inflammation, he had been led to lay stress on the presence of certain large granular cells, "pyrrhol" cells, and therefore examined the reactions of the central nervous system to trypan- and isamin-blue. If the staining material is injected into the blood the choroid plexuses are stained, but the entire nervous system remains free from colouring matter. Thus he believed that the cells of the choroid plexus guard the central nervous system from the action of noxious materials circulating in the blood. When, however, the blue stain is injected into the cerebrospinal fluid the whole of the spinal cord, brain-stem, and optic nerves are deeply stained, and on microscopical section the ganglion-cells in particular are seen to have absorbed the intra-vital coloration. The cerebellum, cerebrum and nerve-roots escape. If the stain is injected into the cerebral subarachnoid space, the colouring material then attacks the cerebral hemispheres.

The author holds that the cerebrospinal fluid carries on the nutritive and excretory functions of the central nervous system, and that the whole of this circulation is guarded by the cells of the choroid plexuses from direct continuity with the blood-stream. In inflammation of the meninges these conditions are changed, and the cerebrospinal fluid and nervous system may be flooded with abnormal substances. Directly the membranes are inflamed the "pyrrhol" cells appear in great numbers and act as phagocytes to the central nervous system.

Zur Psychopathologie des Alltagslebens. Von Prof. Dr. Sigm. Freud. Vierte, vermehrte Auflage. S. 198. Berlin: Karger, 1912.

This is a new edition of Freud's work in which he explains the acts of forgetting, of saying, reading or writing the wrong word, or of choosing the wrong object by normal human beings. Underneath each wrongly performed

act lies an interfering complex. The one common character which underlies all such acts is the repercussion of incompletely suppressed psychical processes which, although not consciously active, have not lost all power to express themselves on the activities of consciousness. A multitude of examples is cited for everyday experience and from European literature.

Papers on Psychoanalysis. By Ernest Jones, M.D., M.R.C.P. Pp. 432. London: Baillière, Tindall and Cox, 1913.

This selection from the author's papers is arranged to follow the main lines of Freud's psychology; but although it begins with an excellent short account of Freud's views, it is occupied mainly with personal experiences of normal and abnormal mental phenomena. Dr. Jones deals with the psychopathology of everyday life, the pathology of morbid anxiety, psychoanalysis in its various forms, amnesia, dreams, and with most of the questions that have been opened up by the work of Freud. The book is extremely well written, and can be strongly recommended to those who wish to gain knowledge of this movement in psychology from the point of view of an ardent disciple.

Der Kopfschmerz. Von Dr. Siegmund Auerbach. S. 132. Berlin: Springer, 1912.

The headaches of primary origin are divided into three groups: migraine, the neurasthenic, and the so-called rheumatic headache. Under migraine the author, like most Continental authorities, includes many periodic and bilateral forms of pain in the head which do not correspond strictly with what is called migraine in this country; for here migraine is usually employed for a form of headache mostly unilateral, and frequently accompanied by fortification-figures, hemianopsia, or other visual phenomena of a high order. The neurasthenic or "fatigue" headache is described, and he then passes on to a form of pain in the head which is scarcely recognized in this country. This is the "rheumatic" ("Knötchen") headache characterized by small thickenings in the connective tissue of the scalp and fascia covering the muscles of the head and neck. The treatment to be employed in such cases is described, and several illustrative clinical histories are given in full. The author then passes to those headaches produced by disease of internal organs; this is the weakest part of the book. He closes with a description of headache in infectious and constitutional diseases.

Lectures on Clinical Psychiatry. By Professor Emil Kraepelin. Authorized Translation from the Second German Edition. Revised and edited by Thomas Johnstone, M.D. Third English Edition. Pp. 368. London: Baillière, Tindall and Cox, 1913.

These are essentially practical clinical demonstrations starting from a given patient, and developing the theme with the help of other examples of the same

disease. The lectures on dementia præcox and katatonia are particularly valuable, whilst every chapter contains many points of interest. The book is preceded by a tabular statement of Kraepelin's Classification of the psychoses. The translation is excellent.

Mind and its Disorders: A Text-book for Students and Practitioners. By W. H. B. STODDART, M.D. Second Edition with illustrations. Pp. 518. London: Lewis, 1912.

This excellent text-book has been brought up to date, and every chapter shows more or less extensive changes and improvements. It can be strongly recommended to students anxious to obtain a knowledge of the physical aspects of mental disease.

Elèments de Sémiologie et Clinique Mentales. Par le Dr. Ph. CHASLIN. Pp. 956. Paris: Asselin et Houzean, 1912.

This text-book is based on the clinical manifestations of insanity, arranged partly under the cause, such as alcohol or organic disease, and partly under such headings as "Folies de persécution," "Folies discordantes," &c. To English readers, interested in the present state of psychiatry, this book will afford many points of comparison with similar works in English and German. The author gives an interesting account from personal experience, of the progress of views on hysteria in Paris from Charcot to the modern school.

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EDITOR.